## (19) World Intellectual Property Organization International Bureau



## 

## (43) International Publication Date 7 December 2000 (07.12.2000)

### **PCT**

# (10) International Publication Number WO 00/73469 A2

- (51) International Patent Classification<sup>7</sup>: C12N 15/54,
   9/12, 15/11, 5/12, C07K 16/40, A61K 38/00, G01N 33/68
- (21) International Application Number: PCT/US00/14842
- (22) International Filing Date: 26 May 2000 (26.05.2000)
- (25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data: 60/136,503

28 May 1999 (28.05.1999) US

- (71) Applicant (for all designated States except US): SUGEN, INC. [US/US]; 230 East Grand Avenue, South San Francisco, CA 94080 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): PLOWMAN, Gregory, D. [US/US]; 4 Honeysuckle Lane, San Carlos, CA 94070 (US). MARTINEZ, Ricardo [US/US]; 984 Cartier Lane, Foster City, CA 94404 (US). WHYTE, David [US/US]; 2623 Barclay Way, Belmont, CA 94002 (US). SUDERSANAM, Sucha [US/US]; 20 Corte Patencio, Greenbrae, CA 94904 (US).

- (74) Agents: WARBURG, Richard, J. et al.; Brobeck, Phleger & Harrison LLP, 12390 El Camino Real, San Diego, CA 92130 (US).
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM). European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, MIL, MR, NE, SN, TD, TG).

#### Published:

 Without international search report and to be republished upon receipt of that report.

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

10/73469 A

(54) Title: PROTEIN KINASES

(57) Abstract: The present invention relates to novel kinase polypeptides, nucleotide sequences encoding the novel kinase polypeptides, as well as various products and methods useful for the diagnosis and treatment of various kinase-related diseases and conditions.

1

# DESCRIPTION PROTEIN KINASES

#### FIELD OF THE INVENTION

5

The present invention relates to novel kinase polypeptides, nucleotide sequences encoding the novel kinase polypeptides, as well as various products and methods useful for the diagnosis and treatment of various kinase-related diseases and conditions.

#### **BACKGROUND OF THE INVENTION**

10

15

The following description of the background of the invention is provided to aid in understanding the invention, but is not admitted to be or to describe prior art to the invention.

Cellular signal transduction is a fundamental mechanism whereby external stimuli that regulate diverse cellular processes are relayed to the interior of cells. One of the key biochemical mechanisms of signal transduction involves the reversible phosphorylation of proteins, which enables regulation of the activity of mature proteins by altering their structure and function.

20

Protein phosphorylation plays a pivotal role in biological signal transduction. Among the biological functions controlled by protein phosphorylation are the following: cell division; differentiation and death (apoptosis); cell motility and cytoskeletal structure; control of DNA replication, transcription, splicing and translation; protein translocation events from the endoplasmic reticulum and Golgi apparatus to the membrane and extracellular space; protein nuclear import and export; regulation of metabolic reactions, etc. Abnormal protein phosphorylation is widely recognized to be causally linked to the etiology of many diseases including cancer as well as immunologic, neuronal and metabolic disorders.

25

The most common phospho-acceptor amino acid residues are serine, threonine and tyrosine. Phosphorylation in histidine has also been observed in bacteria. The presence of a phosphate moeity modulates protein function in multiple ways. A common mechanism includes changes in the catalytic properties ( $V_{max}$  and  $K_m$ ) of an enzyme leading to its activation or inactivation. A second widely recognized mechanism involves promoting protein-protein interactions. An example of this is the tyrosine autophosphorylation of the

30

BNSDOCID: <WO\_\_\_\_\_0073469A2\_I\_>

ligand-activated EGF receptor tyrosine kinase. This event triggers the high-affinity binding to the phosphotyrosine residue on the receptor's C-terminal intracellular domain to the SH2 motif of the adaptor molecule Grb2. Grb2 in turn binds through its SH3 motif to a second adaptor molecule, such as SHC. The formation of this ternary complex activates the signaling events that are responsible for the biological effects of EGF. Serine and threonine phosphorylation events have also being recently recognized to exert their biological function through protein-protein interaction events mediated by the high-affinity binding of phosphoserine and phosphothreonine to WW motifs present in a large variety of proteins (Lu, P.J. et al. (1999) Science 283:1325-1328). A third important outcome of protein phosphorylation is changes in the subcellular localization of the substrate. As an example, nuclear import and export events in a large diversity of proteins are regulated by protein phosphorylation (Drier E.A. et al. (1999) Genes Dev 13: 556-568).

Protein kinases are one of the largest families of eukaryotic proteins with several hundred known members. These proteins share a 250-300 amino acid domain that can be subdivided into 12 distinct subdomains that comprise the common catalytic core structure. These conserved protein motifs have recently been exploited using PCR-based and bioinformatic strategies leading to a significant expansion of the known kinases. Multiple alignment of the sequences in the catalytic domain of protein kinases and subsequent parsimony analysis permits their segregation into a dendrogram reflecting the relatedness of their catalytic domains (Fig. 1). In this manner, related kinases are clustered into distinct branches or subfamilies including: tyrosine kinases, cyclic-nucleotide-dependent kinases, calcium/calmodulin kinases, cyclin-dependent kinases and MAP-kinases, serine-threonine kinase receptors, and several other less defined subfamilies.

We have recently completed a systematic analysis of the protein kinases present in *C. elegans*, the multicellular organism whose entire DNA sequence has been determined. We identified 473 unique kinase profiles including 398 full-length conventional kinases, and 20 additional proteins that may function as atypical protein kinases. (Plowman G.D. *et al.* (1999), Proc. Natl. Acad. Sci. 96:13603-13610).

Using parsimony analysis, the protein kinases may be divided into 4 major groups: AGC, CAMK, CMGC and tyrosine kinases. In addition, there are a number of minor yet distinct families, including the STE and casein kinase 1, families related to worm- or

25

5

10

15

20

fungal-specific kinases, and a family designated "other" to represent several smaller families. In addition, we designate an "atypical" family to represent protein kinases whose catalytic domain has little or no primary sequence homology to conventional kinases, including the A6 kinases and PI3 kinases.

The AGC kinases are basic amino acid-directed enzymes that phosphorylate residues found proximal to Arg and Lys. Examples of this group are the cyclic nucleotide-dependent kinases, G protein kinases, NDR or DBF2 and the ribosomal S6 kinases.

The CAMK group kinases are also basic amino acid-directed kinases. They include the Ca2+/calmodulin-regulated and AMP-dependent protein kinases, myosin light chain kinases, checkpoint 2 kinases (CHK2) and EMK-related protein kinases. The EMK family of STK are involved in the control of cell polarity, micotubule stability and cancer. One member of the EMK family, C-TAK1 has been reported to control entry into mitosis by activating Cdc25C which in turn dephosphorylates Cdc2.

CMGC group kinases are "proline-directed" enzymes phosphorylating residues that exist in a proline-rich context. They include the cyclin-dependent kinases (CDKs), mitogen-activated kinases (MAPKs), GSK3s and CLKs. Most CMGC kinases have larger-than-average kinase domains owing to the presence of insertions within subdomains X and XI.

The tyrosine kinase group encompass both cytoplasmic (i.e. src) as well as transmembrane receptor tyrosine kinases (i.e. EGF receptor). These kinases play a pivotal role in the signal transduction processes that mediate cell proliferation, differentiation and apoptotis.

Group members that define smaller, yet distinct phylogenetic branches of conventional kinases include the elongation factor 2 kinases (EIFKs); homologues of the yeast sterile family kinases (STE) which refers to 3 classes of kinases which lie sequentially upstream of the MAPKs; mixed lineage kinases (MLKs); Lim-domain containing kinases (LIMKs); Calcium-calmodulin kinase kinases (CAMKK), dual-specific tyrosine kinases (DYRK), integrin receptor associated kinase (IRAK); testis-specific kinases (TSK); UNC-51 related kinases (UNC); several families that are close homologues to worm (C26C2.1, YQ09, ZC581.9, YFL033c, C24A1.3), Drosophila (SLOB), or yeast (YDOD\_sp, YGR262\_sc) kinases, and others that are "unique" and don't cluster into any obvious family.

10

5

15

20

25

Ĭ,

5

10

15

20

25

30

### SUMMARY OF THE INVENTION

Through a search of the EST database for homologies to the conserved catalytic kinase domain of protein kinases, hundreds of mammalian members of known and previously unidentified protein kinase families and groups have been identified as part of the present invention. Multiple alignment and parsimony analysis of the catalytic domain reveals that approximately half of these protein kinases cluster into 10 known groups, with the other half perhaps defining novel groups. Classification in this manner has proven highly accurate not only in predicting motifs present in the remaining non-catalytic portion of each protein, but also in their regulation, substrates, and signaling pathways. The present invention includes the partial or complete sequence of new protein kinases, their classification, predicted or deduced protein structure, and a strategy for elucidating their biologic and therapeutic relevance.

Thus, a first aspect of the invention features an isolated, enriched, or purified nucleic acid molecule encoding a kinase polypeptide selected from the group consisting SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136,... SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211,

5

SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

By "isolated" in reference to nucleic acid is meant a polymer of nucleotides conjugated to each other, including DNA and RNA, that is isolated from a natural source or that is synthesized. The isolated nucleic acid of the present invention is unique in the sense that it is not found in a pure or separated state in nature. Use of the term "isolated" indicates that a naturally occurring sequence has been removed from its normal cellular (i.e., chromosomal) environment. Thus, the sequence may be in a cell-free solution or placed in a different cellular environment. The term does not imply that the sequence is the only nucleotide chain present, but that it is essentially free (about 90 - 95% pure at least) of non-nucleotide material naturally associated with it, and thus is distinguished from isolated chromosomes.

By the use of the term "enriched" in reference to nucleic acid is meant that the specific DNA or RNA sequence constitutes a significantly higher fraction (2 - 5 fold) of the total DNA or RNA present in the cells or solution of interest than in normal or diseased cells or in the cells from which the sequence was taken. This could be caused by a person by preferential reduction in the amount of other DNA or RNA present, or by a preferential increase in the amount of the specific DNA or RNA sequence, or by a combination of the two. However, it should be noted that enriched does not imply that there are no other DNA or RNA sequences present, just that the relative amount of the sequence of interest has been significantly increased. The term "significant" is used to indicate that the level of increase is useful to the person making such an increase, and generally means an increase relative to other nucleic acids of about at least 2 fold, more preferably at least 5 to 10 fold or even more. The term also does not imply that there is no DNA or RNA from other sources. The other source DNA may, for example, comprise DNA from a yeast or bacterial genome, or a cloning vector such as pUC19. This term distinguishes from naturally occurring events, such as viral infection, or tumor type

5

10

15

20

25

WO 00/73469

growths, in which the level of one mRNA may be naturally increased relative to other species of mRNA. That is, the term is meant to cover only those situations in which a person has intervened to elevate the proportion of the desired nucleic acid.

It is also advantageous for some purposes that a nucleotide sequence be in purified form. The term "purified" in reference to nucleic acid does not require absolute purity (such as a homogeneous preparation). Instead, it represents an indication that the sequence is relatively more pure than in the natural environment (compared to the natural level this level should be at least 2-5 fold greater, e.g., in terms of mg/mL). Individual clones isolated from a cDNA library may be purified to electrophoretic homogeneity. The claimed DNA molecules obtained from these clones could be obtained directly from total DNA or from total RNA. The cDNA clones are not naturally occurring, but rather are preferably obtained via manipulation of a partially purified naturally occurring substance (messenger RNA). The construction of a cDNA library from mRNA involves the creation of a synthetic substance (cDNA) and pure individual cDNA clones can be isolated from the synthetic library by clonal selection of the cells carrying the cDNA library. Thus, the process which includes the construction of a cDNA library from mRNA and isolation of distinct cDNA clones yields an approximately 10<sup>6</sup>-fold purification of the native message. Thus, purification of at least one order of magnitude, preferably two or three orders, and more preferably four or five orders of magnitude is expressly contemplated.

20

25

30

5

10

15

By a "kinase polypeptide" is meant 10 (preferably 20, more preferably 40, most preferably 75) or more contiguous amino acids set forth in an amino acid sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:168, SEQ ID NO:164, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173,

WO 00/73469 PCT/US00/14842

7

SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEO ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEO ID NO:204, SEO ID NO:205, SEO ID NO:206, SEO ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEO ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or functional derivatives thereof as described herein. For sequences for which the full-length sequence is not given, the remaining sequences can be determined using methods well-known to those in the art and are intended to be included in the invention. In certain aspects, polypeptides of 100, 200, 300 or more amino acids are preferred. The kinase polypeptide can be encoded by a full-length nucleic acid sequence or any portion of the full-length nucleic acid sequence, so long as a functional activity of the polypeptide is retained. By "functional" domain is meant any region of the polypeptide that may play a regulatory or catalytic role as predicted from amino acid sequence homology to other proteins or by the presence of amino acid sequences that may give rise to specific structural conformations (i.e., coiled-coils). For some purposes, polypeptide domains are preferred, including, but not limited to, N-terminal, catalytic/kinase and C-terminal.

The amino acid sequence will be substantially similar to a sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID

5

10

15

20

25

NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID 5 NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID 10 NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEO ID NO:215, SEO ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID 15 NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding full-length amino acid sequence, or fragments thereof. A sequence that is substantially 20 similar to a sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID 25 NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID 30 NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID

NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEO ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEO ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEO ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID 5 NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEO ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID 10 NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEO ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEO ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEO ID NO:242 will have at least 75% identity (preferably 90%, more preferably at least 95% and most preferably 99-100%) to a sequence selected from the group consisting of those 15 set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ 20 ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ 25 ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEO ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ

ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242 or portions of or the entire corresponding full-length amino acid sequences.

10

5

By "identity" is meant a property of sequences that measures their similarity or relationship. Identity is measured by dividing the number of identical residues between two sequences (either full-length or a defined domain) by the total number of residues in the known sequence, or the domain of the known sequence, and multiplying the product by 100. Thus, two copies of exactly the same sequence have 100% identity, but sequences that are less highly conserved, and have replacements and substitutions, have a lower degree of identity. "Gaps" are spaces in an alignment that can result from aligning a novel sequence with a known sequence when the novel sequence has additions or deletions of amino acids in comparison with the known sequence. These gaps do not factor into the assessment of % identity using the sbove calculation.

20

15

Those skilled in the art will recognize that several computer programs are also available for determining sequence identity using standard parameters, for example, Blast (Altschul, et al. (1997) Nucleic Acids Res. 25:3389-3402), Blast2 (Altschul, et al. (1990) J. Mol. Biol. 215:403-410), and Smith-Waterman (Smith, et al. (1981) J. Mol. Biol. 147:195-197).

25

30

In preferred embodiments, the invention features isolated, enriched, or purified nucleic acid molecules encoding a kinase polypeptide comprising a nucleotide sequence that: (a) encodes a polypeptide having an amino acid sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ

WO 00/73469

ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ 5 ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEO ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEO ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEO ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ 10 ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ 15 ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding full-length 20 amino acid sequence, or fragments thereof. A sequence that is substantially similar to a sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEO ID 25 NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEO ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID 30 NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEO ID NO:172, SEO ID

5

10

15

20

25

30

NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEO ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEO ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242 will have at least 75% identity (preferably 90%, more preferably at least 95% and most preferably 99-100%) to the sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID

NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEO ID NO:220, SEO ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID 5 NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242; (b) is the complement of the nucleotide sequence of (a); (c) hybridizes under highly stringent conditions to the nucleotide molecule of (a) and encodes 10 a naturally occurring kinase polypeptide; (d) encodes a kinase polypeptide having an amino acid sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID 15 NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEO ID NO:146, SEO ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID 20 NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID 25 NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID 30 NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEO ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID

NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding full-length amino acid sequence, or fragments thereof. 5 A sequence that is substantially similar to a sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, 10 SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. 15 SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, 20 SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, 25 SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, 30 SEQ ID NO:241, and SEQ ID NO:242 will have at least 75% identity (preferably 90%, more preferably at least 95% and most preferably 99-100%) to the sequence of SEQ ID

NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEO ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID 5 NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID 10 NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEO ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID 15 NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEO ID NO:196, SEO ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID 20 NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ 25 ID NO:242, except that it lacks one or more, but not all, of a domain selected from the group consisting of an N-terminal domain, a catalytic domain, a C-terminal domain, a coiled-coil structure region, a proline-rich region, a spacer region, an insert, and a Cterminal tail; (e) is the complement of the nucleotide sequence of (d); (f) encodes a polypeptide having an amino acid sequence selected from the group consisting of those set 30 forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID

5

10

15

20

25

30

NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEO ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEO ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEO ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEO ID NO:205, SEO ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEO ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding full-length amino acid sequence, or fragments thereof. (The domain demarcations of the polypeptides of the invention are indicated in Table 2 by reference to the kinase domain.) A sequence that is substantially similar to a sequence selected from the group consisting of those set forth in SEO ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID

NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEO ID NO:163, SEO ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEO ID NO:173, SEO ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID 5 NO:182, SEO ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEO ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID 10 NO:207, SEO ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEO ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEO ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEO ID NO:223, SEO ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID 15 NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242 will have at least 75% identity (preferably 90%, more preferably at least 95% and most preferably 99-100%) to the sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ 20 ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ 25 ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEO ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEO ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ 30 ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ

ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ 5 ID NO:211, SEO ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEO ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ 10 ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242; (b) is the complement of the nucleotide sequence of (a); (c) hybridizes under highly stringent conditions to the nucleotide molecule of (a) and encodes a naturally occurring kinase polypeptide; (d) encodes a kinase polypeptide having an amino acid sequence selected from the group consisting of those set forth in SEQ ID 15 NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEO ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEO ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID 20 NO:147, SEO ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID 25 NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID 30 NO:197, SEO ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID

WO 00/73469 PCT/US00/14842

19

NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID 5 NO:232, SEO ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding full-length amino acid sequence, or fragments thereof. A sequence that is substantially similar to a sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, 10 SEO ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEO ID NO:136, SEO ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEO ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEO ID NO:146, SEO ID NO:147, SEO ID NO:148, SEO ID NO:149, SEO ID NO:150, 15 SEO ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEO ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, 20 SEO ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEO ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEO ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEO ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, 25 SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEO ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEO ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, 30 SEO ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEO ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235,

SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEO ID NO:241, and SEQ ID NO:242 will have at least 75% identity (preferably 90%, more preferably at least 95% and most preferably 99-100%) to a domain of a polypeptide selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, 5 SEO ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEO ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, 10 SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEO ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEO ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, 15 SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, 20 SEO ID NO:199, SEO ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, 25 SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, where the domain is selected from the group consisting of an N-terminal domain, a catalytic domain, a C-terminal domain, a coiled-coil structure region, a proline-rich region, a spacer region, 30 an insert, and a C-terminal tail; (g) is the complement of the nucleotide sequence of (f); (h) encodes a polypeptide having an amino acid sequence selected from the group consisting

of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID 5 NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEO ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID 10 NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEO ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID 15 NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID 20 NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEO ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding full-length amino 25 acid sequence, or fragments thereof. A sequence that is substantially similar to a sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEO ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, 30 SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148,

21

PCT/US00/14842

SEO ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEO ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEO ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEO ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEO ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, 5 SEO ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEO ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEO ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEO ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198. 10 SEO ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEO ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEO ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEO ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEO ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, 15 SEO ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEO ID NO:234, SEO ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242 will have at least 75% identity (preferably 90%, more preferably at least 95% and most preferably 99-20 100%) to the sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID 25 NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID 30 NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEO ID NO:173, SEO ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID

WO 00/73469 PCT/US00/14842

23

NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEO ID NO:193, SEO ID NO:194, SEO ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID 5 NO:202, SEO ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID 10 NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242; (b) is the complement of the nucleotide sequence of (a); (c) hybridizes under highly stringent conditions to the nucleotide molecule of (a) and encodes a naturally 15 occurring kinase polypeptide; (d) encodes a kinase polypeptide having an amino acid sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID 20 NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEO ID NO:144, SEO ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEO ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID 25 NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEO ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEO ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID 30 NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID

NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID 5 NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding full-length amino acid sequence, or fragments thereof. A sequence that is 10 substantially similar to a sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEO ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, 15 SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, 20 SEO ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, 25 SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEO ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, 30 SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226,

WO 00/73469 PCT/US00/14842

25

SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEO ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEO ID NO:242 will have at least 75% identity (preferably 90%, more preferably at least 95% and most preferably 99-100%) to the sequence of SEQ ID NO:122, SEQ ID 5 NO:123, SEO ID NO:124, SEO ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEO ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEO ID NO:134, SEO ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID 10 NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEO ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEO ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEO ID NO:164, SEO ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID 15 NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEO ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID 20 NO:198, SEO ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID 25 NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEO ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, except that it lacks one or more of the domains selected from the group consisting of a N-30 terminal domain, a catalytic domain, a C-terminal domain, a coiled-coil structure region, a proline-rich region, a spacer region, an insert, and a C-terminal tail; or (i) is the

complement of the nucleotide sequence of (h). The domain demarcations of the polypeptides of the invention are indicated in Table 2 by reference to the kinase domain.

The term "complement" refers to two nucleotides that can form multiple favorable interactions with one another. For example, adenine is complementary to thymine as they can form two hydrogen bonds. Similarly, guanine and cytosine are complementary since they can form three hydrogen bonds. A nucleotide sequence is the complement of another nucleotide sequence if all of the nucleotides of the first sequence are complementary to all of the nucleotides of the second sequence.

The term "domain" refers to a region of a polypeptide that contains a particular function. For instance, N-terminal or C-terminal domains of signal transduction proteins can serve functions including, but not limited to, binding molecules that localize the signal transduction molecule to different regions of the cell or binding other signaling molecules directly responsible for propagating a particular cellular signal. Some domains can be expressed separately from the rest of the protein and function by themselves, while others must remain part of the intact protein to retain function. The latter are termed functional regions of proteins and also relate to domains.

The term "N-terminal domain" refers to the extracatalytic region located between the initiator methionine and the catalytic domain of the protein kinase. The N-terminal domain can be identified following a Smith-Waterman alignment of the protein sequence against the non-redundant protein database to define the N-terminal boundary of the catalytic domain. Depending on its length, the N-terminal domain may or may not play a regulatory role in kinase function. An example of a protein kinase whose N-terminal domain has been shown to play a regulatory role is PAK65, which contains a CRIB motif used for Cdc42 and rac binding (Burbelo, P.D. et al. (1995) J. Biol. Chem. 270, 29071-29074). The N-terminal domain of a protein kinase of the invention is that portion of the protein kinase to the amino-terminal side of the kinase domain where the kinase domain is identified in Table 2, herein. Further, in some cases, portions of the N-terminal domains of the protein kinases of the invention have not been identified since the entire sequence is not available. However, with the methods described herein, the full-length sequences of the kinases of the invention can be determined and using the approaches described herein the N-terminal domain can be identified.

5

10

15

20

25

The term "catalytic domain" or "kinase domain" refers to a region of the protein kinase that is typically 25-300 amino acids long and is responsible for carrying out the phosphate transfer reaction from a high-energy phosphate donor molecule such as ATP or GTP to itself (autophosphorylation) or to other proteins (exogenous phosphorylation). The catalytic domain of protein kinases is made up of 12 subdomains that contain highly conserved amino acid residues, and are responsible for proper polypeptide folding and for catalysis. The catalytic domain can be identified following a Smith-Waterman alignment of the protein sequence against the non-redundant protein database. The catalytic/kinase domains of the protein kinases of the invention are identified in Table 2, herein. Further, in some cases, the complete sequence of the catalytic/kinase domains of the protein kinases of the invention may not have been provided since the entire sequence is not available. However, with the methods described herein, the full-length sequences of the kinases of the invention can be determined, and using the approaches described herein, the catalytic/kinase domain can be identified.

The term "catalytic activity", as used herein, defines the rate at which a kinase catalytic domain phosphorylates a substrate. Catalytic activity can be measured, for example, by determining the amount of a substrate converted to a phosphorylated product as a function of time. Catalytic activity can be measured by methods of the invention by holding time constant and determining the concentration of a phosphorylated substrate after a fixed period of time. Phosphorylation of a substrate occurs at the active-site of a protein kinase. The active-site is normally a cavity in which the substrate binds to the

The term "substrate" as used herein refers to a molecule phosphorylated by a kinase of the invention. Kinases phosphorylate substrates on serine/threonine or tyrosine amino acids. The molecule may be another protein or a polypeptide.

protein kinase and is phosphorylated.

The term "C-terminal domain" refers to the region located between the catalytic domain and the carboxy-terminal amino acid residue of the protein kinase. The C-terminal domain can be identified by using a Smith-Waterman alignment of the protein sequence against the non-redundant protein database to define the C-terminal boundary of the catalytic domain or of any functional C-terminal extracatalytic domain. Depending on its length and amino acid composition, the C-terminal domain may or may not play a regulatory role in kinase function. An example of a protein kinase whose C-terminal

15

10

5

20

25

30

BNSDOCID: <WO \_\_\_\_\_0073469A2\_I\_>

WO 00/73469 PCT/US00/14842

domain may play a regulatory role is PAK3 which contains a heterotrimeric  $G_b$  subunit-binding site near its C-terminus (Leeuw, T. et al. (1998) Nature, 391, 191-195). The C-terminal domain of a protein kinase of the invention is that portion of the protein kinase to the carboxy-terminal side of the kinase domain where the kinase domain is identified in Table 2, herein. In some cases, the C-terminal domains of the protein kinases of the invention have not been provided since the entire sequence is not available. However, with the methods described herein, the full-length sequences of the kinases of the invention can be determined, and using the approaches described herein, the C-terminal domain can be identified.

10

15

5

The term "signal transduction pathway" refers to the molecules that propagate an extracellular signal through the cell membrane to become an intracellular signal. This signal can then stimulate a cellular response. The polypeptide molecules involved in signal transduction processes are typically receptor and non-receptor protein tyrosine kinases, receptor and non-receptor protein phosphatases, SRC homology 2 and 3 domains, phosphotyrosine binding proteins (SRC homology 2 (SH2) and phosphotyrosine binding (PTB and PH) domain containing proteins), proline-rich binding proteins (SH3 domain containing proteins), nucleotide exchange factors, and transcription factors.

The term "coiled-coil structure region" as used herein, refers to a polypeptide

20

\_

25

30

sequence that has a high probability of adopting a coiled-coil structure as predicted by computer algorithms such as COILS (Lupas, A. (1996) Meth. Enzymology 266:513-525). Coiled-coils are formed by two or three amphipathic α-helices in parallel. Coiled-coils can bind to coiled-coil domains of other polypeptides resulting in homo- or heterodimers (Lupas, A. (1991) Science 252:1162-1164). Coiled-coil-dependent oligomerization has been shown to be necessary for protein function including catalytic activity of serine/threonine kinases (Roe, J. et al. (1997) J. Biol. Chem. 272:5838-5845). Coiled-coil regions in the proteins of the invention can be identified using these methods. They may be present as sub-domains of the N-terminal, kinase, or C-terminal domains of the polypeptides of the invention.

The term "proline-rich region" as used herein, refers to a region of a protein kinase whose proline content over a given amino acid length is higher than the average content of this amino acid found in proteins (i.e., >10%). Proline-rich regions are easily discernable by visual inspection of amino acid sequences and quantitated by standard computer

5

10

15

20

25

30

sequence analysis programs such as the DNAStar program EditSeq. Proline-rich regions have been demonstrated to participate in regulatory protein -protein interactions. Among these interactions, those that are most relevant to this invention involve the "PxxP" proline rich motif found in certain protein kinases (*i.e.*, human PAK1) and the SH3 domain of the adaptor molecule Nck (Galisteo, M.L. *et al.* (1996) J. Biol. Chem. 271:20997-21000). Other regulatory interactions involving "PxxP" proline-rich motifs include the WW domain (Sudol, M. (1996) Prog. Biophys. Mol. Bio. 65:113-132). Proline rich regions in the proteins of the invention can be identified using these methods. They may be present as sub-domains of the N-terminal, kinase, or C-terminal domains of the polypeptides of the invention.

The term "spacer region" as used herein, refers to a region of the protein kinase located between predicted functional domains. The spacer region has no detectable homology to any amino acid sequence in the database, and can be identified by using a Smith-Waterman alignment of the protein sequence against the non-redundant protein database to define the C- and N-terminal boundaries of the flanking functional domains. Spacer regions may or may not play a fundamental role in protein kinase function. Precedence for the regulatory role of spacer regions in kinase function is provided by the role of the src kinase spacer in inter-domain interactions (Xu, W. et al. (1997) Nature 385:595-602). Spacer regions in the proteins of the invention can be identified using these methods. They may be present as sub-domains of the N-terminal, kinase, or C-terminal domains of the polypeptides of the invention.

The term "insert" as used herein refers to a portion of a protein kinase that is absent from a close homolog. Inserts may or may not by the product alternative splicing of exons. Inserts can be identified by using a Smith-Waterman sequence alignment of the protein sequence against the non-redundant protein database, or by means of a multiple sequence alignment of homologous sequences using the DNAStar program Megalign. Inserts may play a functional role by presenting a new interface for protein-protein interactions, or by interfering with such interactions. Insert regions in the proteins of the invention can be identified using these methods. They may be present as sub-domains of the N-terminal, kinase, or C-terminal domains of the polypeptides of the invention.

The term "C-terminal tail" as used herein, refers to a C-terminal domain of a protein kinase, that by homology extends or protrudes past the C-terminal amino acid of its closest homolog. C-terminal tails can be identified by using a Smith-Waterman sequence alignment of the protein sequence against the non-redundant protein database, or by means of a multiple sequence alignment of homologous sequences using the DNAStar program Megalign. Depending on its length, a C-terminal tail may or may not play a regulatory role in kinase function. C-terminal tail regions in the proteins of the invention can be identified using these methods. They may be present as sub-domains of the N-terminal, kinase, or C-terminal domains of the polypeptides of the invention.

10

15

5

Various low or high stringency hybridization conditions may be used depending upon the specificity and selectivity desired. These conditions are well-known to those skilled in the art. Under stringent hybridization conditions only highly complementary nucleic acid sequences hybridize. Preferably, such conditions prevent hybridization of nucleic acids having more than 1 or 2 mismatches out of 20 contiguous nucleotides, more preferably, such conditions prevent hybridization of nucleic acids having more than 1 or 2 mismatches out of 50 contiguous nucleotides, most preferably, such conditions prevent hybridization of nucleic acids having more than 1 or 2 mismatches out of 100 contiguous nucleotides. In some instances, the conditions may prevent hybridization of nucleic acids having more than 5 mismatches in the full-length sequence.

20

25

By stringent hybridization assay conditions is meant hybridization assay conditions at least as stringent as the following: hybridization in 50% formamide, 5X SSC, 50 mM NaH<sub>2</sub>PO<sub>4</sub>, pH 6.8, 0.5% SDS, 0.1 mg/mL sonicated salmon sperm DNA, and 5X Denhart solution at 42 °C overnight; washing with 2X SSC, 0.1% SDS at 45 °C; and washing with 0.2X SSC, 0.1% SDS at 45 °C. Under some of the most stringent hybridization assay conditions, the second wash can be done with 0.1X SSC at a temperature up to 70 °C (pg. 421, Berger et al. (1987) Guide to Molecular Cloning Techniques, Meth. Enzym. vol. 152, hereby incorporated by reference herein including any figures, tables, or drawings.). However, other applications may require the use of conditions falling between these sets of conditions. Methods of determining the conditions required to achieve desired hybridizations are well-known to those with ordinary skill in the art, and are based on several factors, including but not limited to, the sequences to be hybridized and the samples to be tested.

5

10

15

20

25

30

In other preferred embodiments, the invention features isolated, enriched, or purified nucleic acid molecules encoding kinase polypeptides, further comprising a vector or promoter effective to initiate transcription in a host cell. The invention also features recombinant nucleic acid, preferably in a cell or an organism. The recombinant nucleic acid may contain a sequence selected from the group consisting of those set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEO ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEO ID NO:13, SEO ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEO ID NO:18, SEO ID NO:19, SEO ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEO ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEO ID NO:45, SEO ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEO ID NO:50, SEO ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEO ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEO ID NO:77, SEO ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEO ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, and SEQ ID NO:121, or a functional derivative thereof and a vector or a promoter effective to initiate transcription in a host cell. The recombinant nucleic acid can alternatively contain a transcriptional initiation region functional in a cell, a sequence complementary to an RNA sequence encoding a kinase polypeptide and a transcriptional termination region functional in a cell. Specific

vectors and host cell combinations are discussed herein. The recombinant nucleic acid can also contain the full-length sequence encoding the protein kinase, or a domain, for example.

The term "vector" relates to a single or double-stranded circular nucleic acid molecule that can be transfected into cells and replicated within or independently of a cell genome. A circular double-stranded nucleic acid molecule can be cut and thereby linearized upon treatment with restriction enzymes. An assortment of nucleic acid vectors, restriction enzymes, and the knowledge of the nucleotide sequences cut by restriction enzymes are readily available to those skilled in the art. A nucleic acid molecule encoding a kinase can be inserted into a vector by cutting the vector with restriction enzymes and ligating the two pieces together.

The term "transfecting" defines a number of methods to insert a nucleic acid vector or other nucleic acid molecules into a cellular organism. These methods involve a variety of techniques, such as treating the cells with high concentrations of salt, an electric field, detergent, or DMSO to render the outer membrane or wall of the cells permeable to nucleic acid molecules of interest or use of various viral transduction strategies.

The term "promoter" as used herein, refers to nucleic acid sequence needed for gene sequence expression. Promoter regions vary from organism to organism, but are well known to persons skilled in the art for different organisms. For example, in prokaryotes, the promoter region contains both the promoter (which directs the initiation of RNA transcription) as well as the DNA sequences which, when transcribed into RNA, will signal synthesis initiation. Such regions will normally include those 5'-non-coding sequences involved with initiation of transcription and translation, such as the TATA box, capping sequence, CAAT sequence, and the like.

In preferred embodiments, the isolated nucleic acid comprises, consists essentially of, or consists of a nucleic acid sequence set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:35,

25

20

5

10

15

SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID 5 NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ 10 ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, 15 SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, and SEQ ID NO:121, or the corresponding full-length sequence, encodes an amino acid sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID 20 NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID 25 NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID 30 NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEO ID NO:188, SEO ID NO:189, SEO ID NO:190, SEO ID NO:191, SEO ID

WO 00/73469

NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID 5 NO:217, SEO ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEO ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ 10 ID NO:242, or the corresponding full-length amino acid sequence, a functional derivative thereof, or at least 10, 20, 40, 50, 75, 100, 200, 300 or 500 contiguous amino acids of a sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEO ID NO:129, SEO ID NO:130, SEO ID NO:131, SEQ ID NO:132, SEQ ID 15 NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID 20 NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID 25 NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID 30 NO:208, SEO ID NO:209, SEO ID NO:210, SEO ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID

5

10

15

20

25

30

NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding full-length sequences or derivatives thereof. The nucleic acid may be isolated from a natural source by cDNA cloning or by subtractive hybridization. The natural source may be mammalian, preferably human, blood, semen, or tissue, and the nucleic acid may be synthesized by the triester method or by using an automated DNA synthesizer.

The term "mammal" refers preferably to such organisms as mice, rats, rabbits, guinea pigs, sheep, and goats, more preferably to cats, dogs, monkeys, and apes, and most preferably to humans.

In yet other preferred embodiments, the nucleic acid is a conserved or unique region, for example those useful for: the design of hybridization probes to facilitate identification and cloning of additional polypeptides, the design of PCR probes to facilitate cloning of additional polypeptides, obtaining antibodies to polypeptide regions, and designing antisense oligonucleotides.

By "conserved nucleic acid regions", are meant regions present on two or more nucleic acids encoding a kinase polypeptide, to which a particular nucleic acid sequence can hybridize under lower stringency conditions. Examples of lower stringency conditions suitable for screening for nucleic acid encoding kinase polypeptides are provided in Berger *et al.* (1987) Guide to Molecular Cloning Techniques, Meth. Enzym. vol. 152, hereby incorporated by reference herein in its entirety, including any drawings, figures, or tables. Preferably, conserved regions differ by no more than 5 out of 20 nucleotides, even more preferably 2 out of 20 nucleotides or most preferably 1 out of 20 nucleotides.

By "unique nucleic acid region" is meant a sequence present in a nucleic acid coding for a kinase polypeptide that is not present in a sequence coding for any other naturally occurring polypeptide. Such regions preferably encode 10 (preferably 25, more preferably 50, most preferably 75) or more contiguous amino acids selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124,

5

10

15

20

25

30

SEO ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134. SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEO ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEO ID NO:165. SEO ID NO:166, SEO ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEO ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEO ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEO ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEO ID NO:190, SEO ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEO ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEO ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEO ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or functional derivatives thereof. In particular, a unique nucleic acid region is preferably of mammalian origin and preferably human.

A second aspect of the invention features a nucleic acid probe for the detection of nucleic acid encoding a kinase polypeptide in a sample, wherein said polypeptide is selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139,

WO 00/73469 PCT/US00/14842

37

SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEO ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEO ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, 5 SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEO ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEO ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEO ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, 10 SEO ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, 15 SEO ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEO ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, 20 SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242. Preferably, the nucleic acid probe encodes a kinase polypeptide that is a fragment of the protein encoded by an amino acid sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, 25 SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEO ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, 30 SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167,

SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEO ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, 5 SEO ID NO:193, SEO ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, 10 SEO ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID 15 NO:242, or the corresponding full-length amino acid sequences. The nucleic acid probe contains a nucleotide base sequence that will hybridize to a sequence selected from the group consisting of those set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ 20 ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, 25 SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID 30 NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ

ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, and SEQ ID NO:121, or the corresponding full-length sequence, or a functional derivative thereof.

In preferred embodiments, the nucleic acid probe hybridizes to nucleic acid encoding at least 6, 12, 75, 90, 105, 120, 150, 200, 250, 300 or 350 contiguous amino acids of a sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEO ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEO ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID

5

10

15

20

25

5

10

15

20

25

30

NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding full-length amino acid sequence, or functional derivatives thereof.

Methods for using the probes include detecting the presence or amount of kinase RNA in a sample by contacting the sample with a nucleic acid probe under conditions such that hybridization occurs and detecting the presence or amount of the probe bound to kinase RNA. The nucleic acid duplex formed between the probe and a nucleic acid sequence coding for a kinase polypeptide may be used in the identification of the sequence of the nucleic acid detected (Nelson *et al.*, in Nonisotopic DNA Probe Techniques, Academic Press, San Diego, Kricka, ed., p. 275, 1992, hereby incorporated by reference herein in its entirety, including any drawings, figures, or tables). Kits for performing such methods may be constructed to include a container means having disposed therein a nucleic acid probe.

In a third aspect, the invention describes a recombinant cell or tissue comprising a nucleic acid molecule encoding a kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:163, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEO ID NO:182, SEO ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:186, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:1884, SEQ ID NO:185, SEQ ID NO:186,

5

10

15

20

25

30

PCT/US00/14842

41

SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEO ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEO ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242. In such cells, the nucleic acid may be under the control of the genomic regulatory elements, or may be under the control of exogenous regulatory elements including an exogenous promoter. By "exogenous" it is meant a promoter that is not normally coupled in vivo transcriptionally to the coding sequence for the kinase polypeptides.

The polypeptide is preferably a fragment of the protein encoded by an amino acid sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEO ID NO:149, SEO ID NO:150, SEO ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID

NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding full-length amino acid sequence. By "fragment," is meant an amino acid sequence present in a kinase polypeptide. Preferably, such a sequence comprises at least 10, 20, 40, 50, 75, 100, 200, or 300 contiguous amino acids a sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214,

5

10

15

20

25

WO 00/73469 PCT/US00/14842

43

SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or of the corresponding full-length amino acid sequence, or a functional derivative thereof.

In a fourth aspect, the invention features an isolated, enriched, or purified kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ 10 ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEO ID NO:140, SEO ID NO:141, SEO ID NO:142, SEO ID NO:143, SEO ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEO ID NO:150, SEO ID NO:151, SEO ID NO:152, SEO ID NO:153, SEO 15 ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ 20 ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ 25 ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ 30 ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ

ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

By "isolated" in reference to a polypeptide is meant a polymer of amino acids (2 or more amino acids) conjugated to each other, including polypeptides that are isolated from a natural source or that are synthesized. The isolated polypeptides of the present invention are unique in the sense that they are not found in a pure or separated state in nature. Use of the term "isolated" indicates that a naturally occurring sequence has been removed from its normal cellular environment. Thus, the sequence may be in a cell-free solution or placed in a different cellular environment. The term does not imply that the sequence is the only amino acid chain present, but that it is essentially free (about 90 - 95% pure at least) of non-amino acid material naturally associated with it.

By the use of the term "enriched" in reference to a polypeptide is meant that the specific amino acid sequence constitutes a significantly higher fraction (2 - 5 fold) of the total amino acid sequences present in the cells or solution of interest than in normal or diseased cells or in the cells from which the sequence was taken. This could be caused by a person by preferential reduction in the amount of other amino acid sequences present, or by a preferential increase in the amount of the specific amino acid sequence of interest, or by a combination of the two. However, it should be noted that enriched does not imply that there are no other amino acid sequences present, just that the relative amount of the sequence of interest has been significantly increased. The term significant here is used to indicate that the level of increase is useful to the person making such an increase, and generally means an increase relative to other amino acid sequences of about at least 2-fold, more preferably at least 5- to 10-fold or even more. The term also does not imply that there is no amino acid sequence from other sources. The other source of amino acid sequences may, for example, comprise amino acid sequence encoded by a yeast or bacterial genome, or a cloning vector such as pUC19. The term is meant to cover only those situations in which man has intervened to increase the proportion of the desired amino acid sequence.

It is also advantageous for some purposes that an amino acid sequence be in purified form. The term "purified" in reference to a polypeptide does not require absolute purity (such as a homogeneous preparation); instead, it represents an indication that the sequence is relatively purer than in the natural environment. Compared to the natural level

15

10

5

20

25

this level should be at least 2-5 fold greater (e.g., in terms of mg/mL). Purification of at least one order of magnitude, preferably two or three orders, and more preferably four or five orders of magnitude is expressly contemplated. The substance is preferably free of contamination at a functionally significant level, for example 90%, 95%, or 99% pure.

45

PCT/US00/14842

5

10

15

20

25

30

In preferred embodiments, the kinase polypeptide is a fragment of the protein encoded by an amino acid sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEO ID NO:132, SEO ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEO ID NO:157, SEO ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEO ID NO:167, SEO ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEO ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEO ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEO ID NO:202, SEO ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEO ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding full-length amino acid sequences. Preferably, the kinase polypeptide contains at least 10, 20, 40, 50, 75, 100, 200, or 300 contiguous

amino acids a sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEO ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID 5 NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEO ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID 10 NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID 15 NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEO ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID 20 NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ 25 ID NO:242, or the corresponding full-length amino acid sequence, or a functional derivative thereof.

In preferred embodiments, the kinase polypeptide comprises an amino acid sequence having (a) an amino acid sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ

47

PCT/US00/14842

ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ 5 ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEO ID NO:170, SEO ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ 10 ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEO ID NO:190, SEO ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ 15 ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ 20 ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242; (b) an amino acid sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEO ID NO:126, SEO ID NO:127, SEO ID NO:128, SEO ID NO:129, SEO ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ 25 ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ 30 ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ

ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ 5 ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ 10 ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, except that it lacks one or more, but 15 not all, of a domain selected from the group consisting of an N-terminal domain, a catalytic domain, a C-terminal domain, a coiled-coil structure region, a proline-rich region, a spacer region, an insert, and a C-terminal tail; (c) an amino acid sequence of a domain of a polypeptide selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, 20 SEO ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, 25 SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEO ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEO ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, 30 SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187,

WO 00/73469 PCT/US00/14842

SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEO ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, 5 SEO ID NO:213, SEO ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEO ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, 10 SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242 where the domain is selected from the group consisting of an N-terminal domain, a catalytic domain, a C-terminal domain, a coiled-coil structure region, a proline-rich region, a spacer region, an insert, and a C-terminal tail; or (d) an amino acid sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, 15 SEO ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEO ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEO ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, 20 SEO ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163. SEO ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, 25 SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEO ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEO ID NO:189, SEO ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEO ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, 30 SEO ID NO:199, SEO ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEO ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208,

SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, except that it lacks one or more, but not all, of the domains selected from the group consisting of a C-terminal domain, a catalytic domain, an N-terminal domain, a spacer region, a proline-rich region, a coiled-coil structure region, an insert, and a C-terminal tail. (The domain demarcations of the polypeptides of the invention are indicated in Table 2 by reference to the kinase domain.)

The polypeptide can be isolated from a natural source by methods well-known in the art. The natural source may be mammalian, preferably human, blood, semen, or tissue, and the polypeptide may be synthesized using an automated polypeptide synthesizer. The isolated, enriched, or purified kinase polypeptide is preferably selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ

5

10

15

20

25

PCT/US00/14842

51

ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242A.

In some embodiments the invention includes a recombinant kinase polypeptide

10

15

20

25

30

5

selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEO ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229,

5

10

15

20

30

SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEO ID NO:240, SEQ ID NO:241, and SEQ ID NO:242. By "recombinant kinase polypeptide" is meant a polypeptide produced by recombinant DNA techniques such that it is distinct from a naturally occurring polypeptide either in its location (e.g., present in a different cell or tissue than found in nature), purity or structure. Generally, such a recombinant polypeptide will be present in a cell in an amount different from that normally observed in nature.

In a fifth aspect, the invention features an antibody (e.g., a monoclonal or polyclonal antibody) having specific binding affinity to a kinase polypeptide or a kinase polypeptide domain or fragment where the polypeptide is selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEO ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEO ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEO ID NO:147, SEO ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ 25 ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEO ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEO ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEO ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ

ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242. In preferred embodiments, the antibody binds specifically to domains of kinase polypeptides, that are defined *supra*.

By "specific binding affinity" is meant that the antibody binds to the target kinase polypeptide with greater affinity than it binds to other polypeptides under specified conditions. Antibodies or antibody fragments are polypeptides that contain regions that can bind other polypeptides. The term "specific binding affinity" describes an antibody that binds to a kinase polypeptide with greater affinity than it binds to other polypeptides under specified conditions.

The term "polyclonal" refers to antibodies that are heterogenous populations of antibody molecules derived from the sera of animals immunized with an antigen or an antigenic functional derivative thereof. For the production of polyclonal antibodies, various host animals may be immunized by injection with the antigen. Various adjuvants may be used to increase the immunological response, depending on the host species.

"Monoclonal antibodies" are substantially homogenous populations of antibodies to a particular antigen. They may be obtained by any technique which provides for the production of antibody molecules by continuous cell lines in culture. Monoclonal antibodies may be obtained by methods known to those skilled in the art (Kohler *et al.*, Nature 256:495-497, 1975, and U.S. Patent No. 4,376,110, both of which are hereby incorporated by reference herein in their entirety including any figures, tables, or drawings).

The term "antibody fragment" refers to a portion of an antibody, often the hyper variable region and portions of the surrounding heavy and light chains, that displays specific binding affinity for a particular molecule. A hyper variable region is a portion of an antibody that physically binds to the polypeptide target.

Antibodies or antibody fragments having specific binding affinity to a kinase polypeptide or domains of a kinase polypeptide of the invention may be used in methods for detecting the presence and/or amount of kinase polypeptide in a sample by probing the sample with the antibody under conditions suitable for kinase-antibody immunocomplex formation and detecting the presence and/or amount of the antibody conjugated to the

BNSDOCID: <WO\_\_\_\_\_0073469A2\_i\_>

30

25

5

10

15

kinase polypeptide. Diagnostic kits for performing such methods may be constructed to include antibodies or antibody fragments specific for the kinase as well as a conjugate of a binding partner of the antibodies or the antibodies themselves.

An antibody or antibody fragment with specific binding affinity to a kinase polypeptide of the invention can be isolated, enriched, or purified from a prokaryotic or eukaryotic organism. Routine methods known to those skilled in the art enable production of antibodies or antibody fragments, in both prokaryotic and eukaryotic organisms. Purification, enrichment, and isolation of antibodies, which are polypeptide molecules, are described above.

10

15

5

Antibodies having specific binding affinity to a kinase polypeptide of the invention may be used in methods for detecting the presence and/or amount of kinase polypeptide in a sample by contacting the sample with the antibody under conditions such that an immunocomplex forms and detecting the presence and/or amount of the antibody conjugated to the kinase polypeptide. Diagnostic kits for performing such methods may be constructed to include a first container containing the antibody and a second container having a conjugate of a binding partner of the antibody and a label, such as, for example, a radioisotope. The diagnostic kit may also include notification of an FDA approved use and instructions therefor.

20

In a sixth aspect, the invention features a hybridoma which produces an antibody having specific binding affinity to a kinase polypeptide or a kinase polypeptide domain, where the polypeptide is selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:175, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:177, SEQ ID NO:175, SEQ ID NO:175

30

WO 00/73469 PCT/US00/14842

55

NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEO ID NO:229, SEO ID NO:230, SEO ID NO:231, SEO ID NO:232, SEO ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242; and where the domains are defined as above. By "hybridoma" is meant an immortalized cell line that is capable of secreting an antibody, for example an antibody to a kinase of the invention. In preferred embodiments, the antibody to the kinase comprises a sequence of amino acids that is able to specifically bind a kinase polypeptide of the invention.

In a seventh aspect, the invention features a kinase polypeptide binding agent able to bind to a kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187,

5

10

15

20

25

5

10

15

20

25

30

SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEO ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEO ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEO ID NO:203, SEO ID NO:204, SEO ID NO:205, SEO ID NO:206, SEO ID NO:207. SEO ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEO ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEO ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEO ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242. The binding agent is preferably a purified antibody that recognizes an epitope present on a kinase polypeptide of the invention. Other binding agents include molecules that bind to kinase polypeptides and analogous molecules that bind to a kinase polypeptide. Such binding agents may be identified by using assays that measure kinase binding partner activity, such as those that measure PDGFR activity.

The invention also features a method for screening for human cells containing a kinase polypeptide of the invention or an equivalent sequence. The method involves identifying the novel polypeptide in human cells using techniques that are routine and standard in the art, such as those described herein for identifying the kinases of the invention (e.g., cloning, Southern or Northern blot analysis, in situ hybridization, PCR amplification, etc.).

In an eighth aspect, the invention features methods for identifying a substance that modulates kinase activity comprising the steps of: (a) contacting a kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159,

SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEO ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEO ID NO:185, SEO ID NO:186, SEO ID NO:187, SEO ID NO:188, SEO ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199. SEO ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEO ID NO:220, SEO ID NO:221, SEO ID NO:222, SEO ID NO:223, SEO ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEO ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242 with a test substance; (b) measuring the activity of said polypeptide; and (c) determining whether said substance modulates the activity of said polypeptide.

20

25

5

10

15

The term "modulates" refers to the ability of a compound to alter the function of a kinase of the invention. A modulator preferably activates or inhibits the activity of a kinase of the invention.

The term "activates" refers to increasing the cellular activity of the kinase. The term inhibit refers to decreasing the cellular activity of the kinase. Kinase activity is preferably the interaction with a natural binding partner.

The term "modulates" also refers to altering the function of kinases of the invention by increasing or decreasing the probability that a complex forms between the kinase and a natural binding partner. A modulator preferably increases the probability that such a complex forms between the kinase and the natural binding partner, more preferably increases or decreases the probability that a complex forms between the kinase and the natural binding partner depending on the concentration of the compound exposed to the

kinase, and most preferably decreases the probability that a complex forms between the kinase and the natural binding partner.

The term "complex" refers to an assembly of at least two molecules bound to one another. Signal transduction complexes often contain at least two protein molecules bound to one another. For instance, a protein tyrosine receptor protein kinase, GRB2, SOS, RAF, and RAS assemble to form a signal transduction complex in response to a mitogenic ligand.

The term "natural binding partner" refers to polypeptides, lipids, small molecules, or nucleic acids that bind to kinases in cells. A change in the interaction between a kinase and a natural binding partner can manifest itself as an increased or decreased probability that the interaction forms, or an increased or decreased concentration of kinase/natural binding partner complex.

The term "contacting" as used herein refers to mixing a solution comprising the test compound with a liquid medium bathing the cells of the methods. The solution comprising the compound may also comprise another component, such as dimethyl sulfoxide (DMSO), which facilitates the uptake of the test compound or compounds into the cells of the methods. The solution comprising the test compound may be added to the medium bathing the cells by utilizing a delivery apparatus, such as a pipet-based device or syringe-based device.

20

25

30

5

10

15

In a ninth aspect, the invention features methods for identifying a substance that modulates kinase activity in a cell comprising the steps of: (a) expressing a kinase polypeptide in a cell, wherein said polypeptide is selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171,

5

10

15

20

25

30

59

SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176. SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEO ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201. SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEO ID NO:206. SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEO ID NO:241. and SEQ ID NO:242; (b) adding a test substance to said cell; and (c) monitoring a change in cell phenotype or the interaction between said polypeptide and a natural binding partner.

PCT/US00/14842

The term "expressing" as used herein refers to the production of kinases of the invention from a nucleic acid vector containing kinase genes within a cell. The nucleic acid vector is transfected into cells using well known techniques in the art as described herein.

In a tenth aspect, the invention provides methods for treating a disease or abnormal condition by administering to a patient in need of such treatment a substance that modulates the activity of a polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID

5

10

15

20

25

NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEO ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEO ID NO:181, SEO ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEO ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEO ID NO:196, SEO ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEO ID NO:223, SEO ID NO:224, SEO ID NO:225, SEO ID NO:226, SEO ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242. Preferably, the disease is selected from the group consisting of immunerelated diseases and disorders, cardiovascular disease, neurodegenerative disorders, and cancer. Also included are metabolic disorders, such as diabetes mellitus, and reproductive disorders, such as infertility.

Preferably, the disease or disorder is selected from the group consisting of rheumatoid arthritis, artherosclerosis, autoimmune disorders, and organ transplantation. Preferably the disease or disorder is selected from the group consisting of immune-related diseases and disorders, myocardial infarction, cardiomyopathies, stroke, renal failure, and oxidative stress-related neurodegenerative disorders. Most preferably, the immune-related diseases and disorders are selected from the group consisting of rheumatoid arthritis, chronic inflammatory bowel disease, chronic inflammatory pelvic disease, multiple sclerosis, asthma, osteoarthritis, psoriasis, atherosclerosis, rhinitis, autoimmunity, and organ transplantation.

30

Substances useful for treatment of disorders or diseases preferably show positive results in one or more in vitro assays for an activity corresponding to treatment of the disease or disorder in question Substances that modulate the activity of the polypeptides

preferably include, but are not limited to, antisense oligonucleotides and inhibitors of protein kinases.

The term "preventing" refers to decreasing the probability that an organism contracts or develops an abnormal condition.

The term "treating" refers to having a therapeutic effect and at least partially alleviating or abrogating an abnormal condition in the organism.

The term "therapeutic effect" refers to the inhibition or activation factors causing or contributing to the abnormal condition. A therapeutic effect relieves to some extent one or more of the symptoms of the abnormal condition. In reference to the treatment of abnormal conditions, a therapeutic effect can refer to one or more of the following: (a) an increase in the proliferation, growth, and/or differentiation of cells; (b) inhibition (i.e., slowing or stopping) of cell death; (c) inhibition of degeneration; (d) relieving to some extent one or more of the symptoms associated with the abnormal condition; and (e) enhancing the function of the affected population of cells. Compounds demonstrating efficacy against abnormal conditions can be identified as described herein.

The term "abnormal condition" refers to a function in the cells or tissues of an organism that deviates from their normal functions in that organism. An abnormal condition can relate to cell proliferation, cell differentiation or cell survival. An abnormal condition may also include irregularities in cell cycle progression, i.e., irregularities in normal cell cycle progression through mitosis and meiosis.

Abnormal cell proliferative conditions include cancers such as fibrotic and mesangial disorders, abnormal angiogenesis and vasculogenesis, wound healing, psoriasis, diabetes mellitus, and inflammation.

Abnormal differentiation conditions include, but are not limited to neurodegenerative disorders, slow wound healing rates, and slow tissue grafting healing rates.

Abnormal cell survival conditions relate to conditions in which programmed cell death (apoptosis) pathways are activated or abrogated. A number of protein kinases are associated with the apoptosis pathways. Aberrations in the function of any one of the protein kinases could lead to cell immortality or premature cell death.

5

15

10

20

25

30

0073469A2 L >

r"i

The term "aberration", in conjunction with the function of a kinase in a signal transduction process, refers to a kinase that is over- or under-expressed in an organism, mutated such that its catalytic activity is lower or higher than wild-type protein kinase activity, mutated such that it can no longer interact with a natural binding partner, is no longer modified by another protein kinase or protein phosphatase, or no longer interacts with a natural binding partner.

The term "administering" relates to a method of incorporating a compound into cells or tissues of an organism. The abnormal condition can be prevented or treated when the cells or tissues of the organism exist within the organism or outside of the organism. Cells existing outside the organism can be maintained or grown in cell culture dishes. For cells harbored within the organism, many techniques exist in the art to administer compounds, including (but not limited to) oral, parenteral, dermal, injection, and aerosol applications. For cells outside of the organism, multiple techniques exist in the art to administer the compounds, including (but not limited to) cell microinjection techniques, transformation techniques, and carrier techniques.

The abnormal condition can also be prevented or treated by administering a compound to a group of cells having an aberration in a signal transduction pathway to an organism. The effect of administering a compound on organism function can then be monitored. The organism is preferably a mouse, rat, rabbit, guinea pig, or goat, more preferably a monkey or ape, and most preferably a human.

In an eleventh aspect, the invention features methods for detection the expression of a polypeptide in a sample as a diagnostic tool for diseases or disorders, wherein the method comprises the steps of: (a) contacting the sample with a nucleic acid probe which hybridizes under hybridization assay conditions to a nucleic acid target region of a kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:158, SEQ

20

25

30

5

10

15

BNSDOCID: <WO\_\_\_\_\_0073469A2\_I\_>

5

10

15

20

25

30

ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEO ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEO ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEO ID NO:200, SEO ID NO:201, SEO ID NO:202, SEO ID NO:203, SEO ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEO ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEO ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEO ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, said probe comprising the nucleic acid sequence encoding the polypeptide, fragments thereof, and the complements of the sequences and fragments; and (b) detecting the presence or amount of the probe:target region hybrid as an indication of the disease.

In preferred embodiments of the invention, the disease or disorder is selected from the group consisting of rheumatoid arthritis, artherosclerosis, autoimmune disorders, organ transplantation, myocardial infarction, cardiomyopathies, stroke, renal failure, oxidative stress-related neurodegenerative disorders, metabolic disorder including diabetes, reproductive disorders including infertility, and cancer.

The kinase "target region" is a nucleotide base sequence selected from the group consisting of those set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID

5

10

15

20

25

30

NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEO ID NO:37, SEO ID NO:38, SEO ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEO ID NO:69, SEO ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEO ID NO:101, SEO ID NO:102, SEO ID NO:103, SEO ID NO:104, SEO ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, and SEO ID NO:121, or the corresponding full-length sequences, a functional derivative thereof, or a fragment thereof to which the nucleic acid probe will specifically hybridize. Specific hybridization indicates that in the presence of other nucleic acids the probe only hybridizes detectably with the kinase of the invention's target region. Putative target regions can be identified by methods well known in the art consisting of alignment and comparison of the most closely related sequences in the database.

In preferred embodiments the nucleic acid probe hybridizes to a kinase target region encoding at least 6, 12, 75, 90, 105, 120, 150, 200, 250, 300 or 350 contiguous amino acids of the sequence set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID

NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEO ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEO ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEO ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEO ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or the corresponding full-length amino acid sequence, or a functional derivative thereof. Hybridization conditions should be such that hybridization occurs only with the kinase genes in the presence of other nucleic acid molecules. Under stringent hybridization conditions only highly complementary nucleic acid sequences hybridize. Preferably, such conditions prevent hybridization of nucleic acids having more than 1 or 2 mismatches out of 20 contiguous nucleotides. Such conditions are defined supra.

25

20

5

10

15

Hybridization conditions should be such that hybridization occurs only with the genes in the presence of other nucleic acid molecules. Under stringent hybridization conditions only highly complementary nucleic acid sequences hybridize. Preferably, such conditions prevent hybridization of nucleic acids having 1 or 2 mismatches out of 20 contiguous nucleotides. Such conditions are defined *supra*.

30

The diseases for which detection of kinase genes in a sample could be diagnostic include diseases in which kinase nucleic acid (DNA and/or RNA) is amplified in comparison to normal cells. By "amplification" is meant increased numbers of kinase

PCT/US00/14842

66

DNA or RNA in a cell compared with normal cells. In normal cells, kinases are typically found as single copy genes. In selected diseases, the chromosomal location of the kinase genes may be amplified, resulting in multiple copies of the gene, or amplification. Gene amplification can lead to amplification of kinase RNA, or kinase RNA can be amplified in the absence of kinase DNA amplification.

"Amplification" as it refers to RNA can be the detectable presence of kinase RNA in cells, since in some normal cells there is no basal expression of kinase RNA. In other normal cells, a basal level of expression of kinase exists, therefore in these cases amplification is the detection of at least 1-2-fold, and preferably more, kinase RNA, compared to the basal level.

The diseases that could be diagnosed by detection of kinase nucleic acid in a sample preferably include cancers. The test samples suitable for nucleic acid probing methods of the present invention include, for example, cells or nucleic acid extracts of cells, or biological fluids. The samples used in the above-described methods will vary based on the assay format, the detection method and the nature of the tissues, cells or extracts to be assayed. Methods for preparing nucleic acid extracts of cells are well known in the art and can be readily adapted in order to obtain a sample that is compatible with the method utilized.

Another aspect of the invention involves a method of agonizing (stimulating) or antagonizing a target of the invention and a natural binding partner associated activity in a mammal comprising administering to said mammal an agonist or antagonist to one of the above disclosed polypeptides in an amount sufficient to effect said agonism or antagonism. A method of treating diseases in a mammal with an agonist or antagonist of the protein of the present invention activity comprising administering the agonist or antagonist to a mammal in an amount sufficient to agonize or antagonize associated functions is also encompassed in the present application.

In an effort to discover novel treatments for diseases, biomedical researchers and chemists have designed, synthesized, and tested molecules that inhibit the function of protein polypeptides. Some small organic molecules form a class of compounds that modulate the function of protein polypeptides. Examples of molecules that have been reported to inhibit the function of protein kinases include, but are not limited to, bis monocyclic, bicyclic or heterocyclic aryl compounds (PCT WO 92/20642, published

10

5

15

20

25

November 26, 1992 by Maguire et al.), vinylene-azaindole derivatives (PCT WO 94/14808, published July 7, 1994 by Ballinari et al.), 1-cyclopropyl-4-pyridyl-quinolones (U.S. Patent No. 5,330,992), styryl compounds (U.S. Patent No. 5,217,999), styryl-substituted pyridyl compounds (U.S. Patent No. 5,302,606), certain quinazoline derivatives (EP Application No. 0 566 266 A1), seleoindoles and selenides (PCT WO 94/03427, published February 17, 1994 by Denny et al.), tricyclic polyhydroxylic compounds (PCT WO 92/21660, published December 10, 1992 by Dow), and benzylphosphonic acid compounds (PCT WO 91/15495, published October 17, 1991 by Dow et al), all of which are incorporated by reference herein, including any drawings.

10

5

Compounds that can traverse cell membranes and are resistant to acid hydrolysis are potentially advantageous as therapeutics as they can become highly bioavailable after being administered orally to patients. However, many of these protein inhibitors only weakly inhibit function. In addition, many inhibit a variety of protein kinases and will therefore cause multiple side-effects as therapeutics for diseases.

Some indolinone compounds, however, form classes of acid resistant and

15

20

25

membrane permeable organic molecules. WO 96/22976 (published August 1, 1996 by Ballinari et al.) describes hydrosoluble indolinone compounds that harbor tetralin, naphthalene, quinoline, and indole substituents fused to the oxindole ring. These bicyclic substituents are in turn substituted with polar groups including hydroxylated alkyl, phosphate, and ether substituents. U.S. Patent Application Serial Nos. 08/702,232, filed August 23, 1996, entitled "Indolinone Combinatorial Libraries and Related Products and Methods for the Treatment of Disease" by Tang et al. (Lyon & Lyon Docket No. 221/187) and 08/485,323, filed June 7, 1995, entitled "Benzylidene-Z-Indoline Compounds for the Treatment of Disease" by Tang et al. (Lyon & Lyon Docket No. 223/298) and International Patent Publication WO 96/22976, published August 1, 1996 by Ballinari et al., all of which are incorporated herein by reference in their entirety, including any drawings, describe indolinone chemical libraries of indolinone compounds harboring other bicyclic moieties as well as monocyclic moieties fused to the oxindole ring. Applications 08/702,232, filed August 23, 1996, entitled "Indolinone Combinatorial Libraries and Related Products and Methods for the Treatment of Disease" by Tang et al. (Lyon & Lyon Docket No. 221/187), 08/485,323, filed June 7, 1995, entitled "Benzylidene-Z-Indoline Compounds for the Treatment of Disease" by Tang et al. (Lyon

& Lyon Docket No. 223/298), and WO 96/22976, published August 1, 1996 by Ballinari et al. teach methods of indolinone synthesis, methods of testing the biological activity of indolinone compounds in cells, and inhibition patterns of indolinone derivatives, both of which are incorporated by reference herein, including any drawings.

5

10

15

Other examples of substances capable of modulating kinase activity include, but are not limited to, tyrphostins, quinazolines, quinoxolines, and quinolines. The quinazolines, tyrphostins, quinolines, and quinoxolines referred to above include well known compounds such as those described in the literature. For example, representative publications describing quinazolines include Barker et al., EPO Publication No. 0 520 722 A1; Jones et al., U.S. Patent No. 4,447,608; Kabbe et al., U.S. Patent No. 4,757,072; Kaul and Vougioukas, U.S. Patent No. 5, 316,553; Kreighbaum and Comer, U.S. Patent No. 4,343,940; Pegg and Wardleworth, EPO Publication No. 0 562 734 A1; Barker et al., Proc. of Am. Assoc. for Cancer Research 32:327 (1991); Bertino, J.R., Cancer Research 3:293-304 (1979); Bertino, J.R., Cancer Research 9(2 part 1):293-304 (1979); Curtin et al., Br. J. Cancer 53:361-368 (1986); Fernandes et al., Cancer Research 43:1117-1123 (1983); Ferris et al. J. Org. Chem. 44(2):173-178; Fry et al., Science 265:1093-1095 (1994); Jackman et al., Cancer Research 51:5579-5586 (1981); Jones et al. J. Med. Chem. 29(6):1114-1118; Lee and Skibo, Biochemistry 26(23):7355-7362 (1987); Lemus et al., J. Org. Chem. 54:3511-3518 (1989); Ley and Seng, Synthesis 1975:415-522 (1975); Maxwell et al., Magnetic Resonance in Medicine 17:189-196 (1991); Mini et al., Cancer Research 45:325-330 (1985); Phillips and Castle, <u>J. Heterocyclic Chem.</u> 17(19):1489-1596 (1980); Reece et al., Cancer Research 47(11):2996-2999 (1977); Sculier et al., Cancer Immunol. and Immunother. 23:A65 (1986); Sikora et al., Cancer Letters 23:289-295 (1984); and Sikora et al., Analytical Biochem. 172:344-355 (1988), all of which are incorporated

20

25

Quinoxaline is described in Kaul and Vougioukas, U.S. Patent No. 5,316,553, incorporated herein by reference in its entirety, including any drawings.

herein by reference in their entirety, including any drawings.

Quinolines are described in Dolle et al., <u>J. Med. Chem.</u> 37:2627-2629 (1994); MaGuire, <u>J. Med. Chem.</u> 37:2129-2131 (1994); Burke et al., <u>J. Med. Chem.</u> 36:425-432 (1993); and Burke et al. <u>BioOrganic Med. Chem. Letters</u> 2:1771-1774 (1992), all of which are incorporated by reference in their entirety, including any drawings.

Tyrphostins are described in Allen et al., Clin. Exp. Immunol. 91:141-156 (1993); Anafi et al., Blood 82:12:3524-3529 (1993); Baker et al., J. Cell Sci. 102:543-555 (1992); Bilder et al., Amer. Physiol. Soc. pp. 6363-6143:C721-C730 (1991); Brunton et al., Proceedings of Amer. Assoc. Cancer Rsch. 33:558 (1992); Bryckaert et al., Experimental Cell Research 199:255-261 (1992); Dong et al., J. Leukocyte Biology 53:53-60 (1993); Dong et al., J. Immunol. 151(5):2717-2724 (1993); Gazit et al., J. Med. Chem. 32:2344-2352 (1989); Gazit et al., "J. Med. Chem. 36:3556-3564 (1993); Kaur et al., Anti-Cancer Drugs 5:213-222 (1994); Kaur et al., King et al., Biochem. J. 275:413-418 (1991); Kuo et al., Cancer Letters 74:197-202 (1993); Levitzki, A., The FASEB J. 6:3275-3282 (1992); Lyall et al., J. Biol. Chem. 264:14503-14509 (1989); Peterson et al., The Prostate 22:335-345 (1993); Pillemer et al., Int. J. Cancer 50:80-85 (1992); Posner et al., Molecular Pharmacology 45:673-683 (1993); Rendu et al., Biol. Pharmacology 44(5):881-888 (1992); Sauro and Thomas, Life Sciences 53:371-376 (1993); Sauro and Thomas, <u>J.</u> Pharm. and Experimental Therapeutics 267(3):119-1125 (1993); Wolbring et al., J. Biol. Chem. 269(36):22470-22472 (1994); and Yoneda et al., Cancer Research 51:4430-4435 (1991); all of which are incorporated herein by reference in their entirety, including any drawings.

Other compounds that could be used as modulators include oxindolinones such as those described in U.S. patent application Serial No. 08/702,232 filed August 23, 1996, incorporated herein by reference in its entirety, including any drawings.

Methods of Treating a Disease (Enablement - i.e., Dosing)

Methods of determining the dosages of compounds to be administered to a patient and modes of administering compounds to an organism are disclosed in U.S. Application Serial No. 08/702,282, filed August 23, 1996 and International patent publication number WO 96/22976, published August 1 1996, both of which are incorporated herein by reference in their entirety, including any drawings, figures or tables. Those skilled in the art will appreciate that such descriptions are applicable to the present invention and can be easily adapted to it.

The proper dosage depends on various factors such as the type of disease being treated, the particular composition being used and the size and physiological condition of the patient. Therapeutically effective doses for the compounds described herein can be estimated initially from cell culture and animal models. For example, a dose can be

5

10

15

20

WO 00/73469 PCT/US00/14842

70

formulated in animal models to achieve a circulating concentration range that initially takes into account the  $IC_{50}$  as determined in cell culture assays. The animal model data can be used to more accurately determine useful doses in humans.

Plasma half-life and biodistribution of the drug and metabolites in the plasma, tumors and major organs can also be determined to facilitate the selection of drugs most appropriate to inhibit a disorder. Such measurements can be carried out. For example, HPLC analysis can be performed on the plasma of animals treated with the drug and the location of radiolabeled compounds can be deter-mined using detection methods such as X-ray, CAT scan and MRI. Compounds that show potent inhibitory activity in the screening assays, but have poor pharmacokinetic characteristics, can be optimized by altering the chemical structure and retesting. In this regard, compounds displaying good pharmacokinetic characteristics can be used as a model.

Toxicity studies can also be carried out by measuring the blood cell composition. For example, toxicity studies can be carried out in a suitable animal model as follows:

1) the compound is administered to mice (an untreated control mouse should also be used); 2) blood samples are periodically obtained via the tail vein from one mouse in each treatment group; and 3) the samples are analyzed for red and white blood cell counts, blood cell composition and the percent of lymphocytes versus polymorphonuclear cells. A comparison of results for each dosing regime with the controls indicates if toxicity is present.

At the termination of each toxicity study, further studies can be carried out by sacrificing the animals (preferably, in accordance with the American Veterinary Medical Association guidelines Report of the American Veterinary Medical Assoc. Panel on Euthanasia, Journal of American Veterinary Medical Assoc., 202:229-249, 1993). Representative animals from each treatment group can then be examined by gross necropsy for immediate evidence of metastasis, unusual illness or toxicity. Gross abnormalities in tissue are noted and tissues are examined histologically. Compounds causing a reduction in body weight or blood components are less preferred, as are compounds having an adverse effect on major organs. In general, the greater the adverse effect the less preferred the compound.

30

25

5

10

15

20

BNSDOCID: <WO

0073469A2 I >

WO 00/73469 PCT/US00/14842

71

For the treatment of cancers the expected daily dose of a hydrophobic pharmaceutical agent is between 1 to 500 mg/day, preferably 1 to 250 mg/day, and most preferably 1 to 50 mg/day. Drugs can be delivered less frequently provided plasma levels of the active moiety are sufficient to maintain therapeutic effectiveness.

5

10

15

20

25

30

Plasma levels should reflect the potency of the drug. Generally, the more potent the compound the lower the plasma levels necessary to achieve efficacy.

In a final aspect, the invention features a method for detection of a kinase polypeptide in a sample as a diagnostic tool for a disease or disorder, wherein the method comprises: (a) comparing a nucleic acid target region encoding the kinase polypeptide in a sample, where the kinase polypeptide is selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEO ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEO ID NO:146, SEO ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEO ID NO:181, SEO ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEO ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEO ID NO:211, SEO ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID

10

15

20

25

NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or one or more fragments thereof, with a control nucleic acid target region encoding the kinase polypeptide, or one or more fragments thereof; and (b) detecting differences in sequence or amount between the target region and the control target region, as an indication of the disease or disorder. Preferably, the disease or disorder is selected from the group consisting of immune-related diseases and disorders, organ transplantation, myocardial infarction, cardiovascular disease, stroke, renal failure, oxidative stress-related neurodegenerative disorders, and cancer. Immune-related diseases and disorders include, but are not limited to, those discussed previously.

The term "comparing" as used herein refers to identifying discrepancies between the nucleic acid target region isolated from a sample, and the control nucleic acid target region. The discrepancies can be in the nucleotide sequences, e.g. insertions, deletions, or point mutations, or in the amount of a given nucleotide sequence. Methods to determine these discrepancies in sequences are well-known to one of ordinary skill in the art. The "control" nucleic acid target region refers to the sequence or amount of the sequence found in normal cells, e.g. cells that are not diseased as discussed previously.

The term also includes anti-sense molecules drawn thereto.

The invention has been described broadly and generically herein. Each of the narrower species and subgeneric groupings falling within the generic disclosure also form part of the invention. This includes the generic description of the invention with a proviso or negative limitation removing any subject matter from the genus, regardless of whether or not the excised material is specifically recited herein. For example, in some instances the nucleotide sequence of particular kinase polypeptides may not be part of a preferred embodiment.

The summary of the invention described above is not limiting and other features and advantages of the invention will be apparent from the following detailed description of the invention, and from the claims.

WO 00/73469 PCT/US00/14842

73

### BRIEF DESCRIPTION OF THE FIGURES

Figures 1A to 1BB shows the amino acid sequences of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

Figures 2A to 2MMMM shows the nucleic acid sequences of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID

5

10

15

20

25

NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEO ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEO ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEO ID NO:44, SEO ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEO ID NO:55. SEO ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEO ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEO ID NO:76, SEO ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEO ID NO:87, SEO ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEO ID NO:92, SEO ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103. SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, and SEQ ID NO:121.

20

25

15

5

10

## DETAILED DESCRIPTION OF THE INVENTION

The present invention relates in part to kinase polypeptides, nucleic acids encoding such polypeptides, cells containing such nucleic acids, antibodies to such polypeptides, assays utilizing such polypeptides, and methods relating to all of the foregoing. The present invention is based upon the isolation and characterization of new kinase polypeptides. The polypeptides and nucleic acids may be produced using well-known and standard synthesis techniques when given the sequences presented herein.

# I. The Nucleic Acids of the Invention

Included within the scope of this invention are the functional equivalents of the herein-described isolated nucleic acid molecules. The degeneracy of the genetic code permits substitution of certain codons by other codons that specify the same amino acid and hence would give rise to the same protein. The nucleic acid sequence can vary

substantially since, with the exception of methionine and tryptophan, the known amino acids can be coded for by more than one codon. Thus, portions or all of the kinase genes of the invention could be synthesized to give a nucleic acid sequence significantly different from one selected from the group consisting of those set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEO ID NO:43, SEO ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, and SEQ ID NO:121. The encoded amino acid sequence thereof would, however, be preserved.

In addition, the nucleic acid sequence may comprise a nucleotide sequence which results from the addition, deletion or substitution of at least one nucleotide to the 5'-end and/or the 3'-end of the nucleic acid sequence shown in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID

5

10

15

20

25

NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13. SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEO ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEO ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEO ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ 5 ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEO ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45. SEO ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, 10 SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEO ID NO:66, SEO ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEO ID NO:78, SEO ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ 15 ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEO ID NO:93. SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEO ID 20 NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, and SEQ ID NO:121, or a derivative thereof. Any nucleotide or polynucleotide may be used in this regard, provided that its addition, deletion or substitution does not alter the amino acid sequence of SEQ ID NO:122, SEQ ID NO:123, 25 SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEO ID NO:128. SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, 30 SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEO ID NO:153. SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEO ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163,

10

15

20

25

30

SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168. SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178. SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183. SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188. SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193. SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEO ID NO:198. SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203. SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213. SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223. SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEO ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, that is encoded by the nucleotide sequence. For example, the present invention is intended to include any nucleic acid sequence resulting from the addition of ATG as an initiation codon at the 5'end of the inventive nucleic acid sequence or its derivative, or from the addition of TTA, TAG or TGA as a termination codon at the 3'-end of the inventive nucleotide sequence or its derivative. Moreover, the nucleic acid molecule of the present invention may, as necessary, have restriction endonuclease recognition sites added to its 5'-end and/or 3'end.

Such functional alterations of a given nucleic acid sequence afford an opportunity to promote secretion and/or processing of heterologous proteins encoded by foreign nucleic acid sequences fused thereto, for example. All variations of the nucleotide sequence of the kinase genes of the invention and fragments thereof permitted by the genetic code are, therefore, included in this invention.

Further, it is possible to delete codons or to substitute one or more codons with codons other than degenerate codons to produce a structurally modified polypeptide, but one which has substantially the same utility or activity as the polypeptide produced by the unmodified nucleic acid molecule. As recognized in the art, the two polypeptides are

functionally equivalent, as are the two nucleic acid molecules that give rise to their production, even though the differences between the nucleic acid molecules are not related to the degeneracy of the genetic code. This is discussed further in the "Functional Derivatives" section, herein.

5

Finally, many of the nucleic acid molecules of the invention are provided as a partial sequence only (Fig. 2A through 2QQ). However, it is standard for one of ordinary skill in the art to obtain a full-length sequence when provided with a partial sequence. Similarly, when provided with a partial or full-length sequence it is standard for one of ordinary skill in the art to obtain nucleic acid sequence coding for homologous proteins. Therefore, these nucleic acid molecules are also part of the invention.

10

The characteristics of the protein kinase nucleic acid sequences of the invention are provided in Table 1. The protein kinases fall into 10 known groups: AGC, CAMK, CKI, CMGC, dsPK, EIFK, LIMK, MLK, STE and TK. In addition, there are a significant number of protein kinases that do not belong to any of the known groups, and therefore presumably define new protein kinase groups.

15

Additional characteristics may be found, *inter alia*, in the tables, namely Table 1, Table 2, Table 3 and Table 4, shown below.

# II. <u>Nucleic Acid Probes, Methods, and Kits for Detection of Protein Kinases.</u>

20

A nucleic acid probe of the present invention may be used to probe an appropriate chromosomal or cDNA library by usual hybridization methods to obtain other nucleic acid molecules of the present invention. A chromosomal DNA or cDNA library may be prepared from appropriate cells according to recognized methods in the art (cf. "Molecular Cloning: A Laboratory Manual", second edition, Cold Spring Harbor Laboratory, Sambrook, Fritsch, & Maniatis, eds., 1989).

25

In the alternative, chemical synthesis can be carried out in order to obtain nucleic acid probes having nucleotide sequences that correspond to N-terminal, kinase or C-terminal portions, for example, of the amino acid sequence of the polypeptide of interest. The synthesized nucleic acid probes may be used as primers in a polymerase chain reaction (PCR) carried out in accordance with recognized PCR techniques, essentially according to PCR Protocols, "A Guide to Methods and Applications", Academic Press,

WO 00/73469 PCT/US00/14842

79

Michael, et al., eds., 1990, utilizing the appropriate chromosomal or cDNA library to obtain the fragment of the present invention.

One skilled in the art can readily design such probes based on the sequence disclosed herein using methods of computer alignment and sequence analysis known in the art ("Molecular Cloning: A Laboratory Manual", 1989, supra). The hybridization probes of the present invention can be labeled by standard labeling techniques such as with a radiolabel, enzyme label, fluorescent label, biotin-avidin label, chemiluminescence, and the like. After hybridization, the probes may be visualized using known methods.

The nucleic acid probes of the present invention include RNA, as well as DNA probes, such probes being generated using techniques known in the art. The nucleic acid probe may be immobilized on a solid support. Examples of such solid supports include, but are not limited to, plastics such as polycarbonate, complex carbohydrates such as agarose and sepharose, and acrylic resins, such as polyacrylamide and latex beads. Techniques for coupling nucleic acid probes to such solid supports are well known in the art.

The test samples suitable for nucleic acid probing methods of the present invention include, for example, cells or nucleic acid extracts of cells, or biological fluids. The samples used in the above-described methods will vary based on the assay format, the detection method and the nature of the tissues, cells or extracts to be assayed. Methods for preparing nucleic acid extracts of cells are well known in the art and can be readily adapted in order to obtain a sample that is compatible with the method utilized.

One method of detecting the presence of nucleic acids of the invention in a sample comprises (a) contacting said sample with the above-described nucleic acid probe under conditions such that hybridization occurs, and (b) detecting the presence of said probe bound to said nucleic acid molecule. One skilled in the art would select the nucleic acid probe according to techniques known in the art as described above. Samples to be tested include but should not be limited to RNA samples of human tissue.

A kit for detecting the presence of nucleic acids of the invention in a sample comprises at least one container means having disposed therein the above-described nucleic acid probe. The kit may further comprise other containers comprising one or more of the following: wash reagents and reagents capable of detecting the presence of bound nucleic acid probe. Examples of detection reagents include, but are not limited to

30

25

5

10

15

radiolabelled probes, enzymatic labeled probes (horseradish peroxidase, alkaline phosphatase), and affinity labeled probes (biotin, avidin, or steptavidin).

In detail, a compartmentalized kit includes any kit in which reagents are contained in separate containers. Such containers include small glass containers, plastic containers or strips of plastic or paper. Such containers allow the efficient transfer of reagents from one compartment to another compartment such that the samples and reagents are not cross-contaminated and the agents or solutions of each container can be added in a quantitative fashion from one compartment to another. Such containers will include a container which will accept the test sample, a container which contains the probe or primers used in the assay, containers which contain wash reagents (such as phosphate buffered saline, Tris-buffers, and the like), and containers which contain the reagents used to detect the hybridized probe, bound antibody, amplified product, or the like. One skilled in the art will readily recognize that the nucleic acid probes described in the present invention can readily be incorporated into one of the established kit formats that are well known in the art.

# III. DNA Constructs Comprising a Protein Kinase Nucleic Acid Molecule and Cells Containing These Constructs.

The present invention also relates to a recombinant DNA molecule comprising, 5' to 3', a promoter effective to initiate transcription in a host cell and the above-described nucleic acid molecules. In addition, the present invention relates to a recombinant DNA molecule comprising a vector and an above-described nucleic acid molecule. The present invention also relates to a nucleic acid molecule comprising a transcriptional region functional in a cell, a sequence complementary to an RNA sequence encoding an amino acid sequence corresponding to the above-described polypeptide, and a transcriptional termination region functional in said cell. The above-described molecules may be isolated and/or purified DNA molecules.

The present invention also relates to a cell or organism that contains an above-described nucleic acid molecule and thereby is capable of expressing a polypeptide. The polypeptide may be purified from cells that have been altered to express the polypeptide. A cell is said to be "altered to express a desired polypeptide" when the cell, through genetic manipulation, is made to produce a protein which it normally does not produce or

30

25

5

10

15

20

**見さらくこう・ > とう** 

007346042 I >

WO 00/73469 PCT/US00/14842

81

which the cell normally produces at lower levels. One skilled in the art can readily adapt procedures for introducing and expressing either genomic, cDNA, or synthetic sequences into either eukaryotic or prokaryotic cells.

A nucleic acid molecule, such as DNA, is said to be "capable of expressing" a polypeptide if it contains nucleotide sequences which contain transcriptional and translational regulatory information and such sequences are "operably linked" to nucleotide sequences which encode the polypeptide. An operable linkage is a linkage in which the regulatory DNA sequences and the DNA sequence sought to be expressed are connected in such a way as to permit gene sequence expression. The precise nature of the regulatory regions needed for gene sequence expression may vary from organism to organism, but shall in general include a promoter region which, in prokaryotes, contains both the promoter (which directs the initiation of RNA transcription) as well as the DNA sequences which, when transcribed into RNA, will signal synthesis initiation. Such regions will normally include those 5'-non-coding sequences involved with initiation of transcription and translation, such as the TATA box, capping sequence, CAAT sequence, and the like.

If desired, the non-coding region 3' to the sequence encoding a kinase of the invention may be obtained by the above-described methods. This region may be retained for its transcriptional termination regulatory sequences, such as termination and polyadenylation. Thus, by retaining the 3'-region naturally contiguous to the DNA sequence encoding a kinase of the invention, the transcriptional termination signals may be provided. Where the transcriptional termination signals are not satisfactorily functional in the expression host cell, then a 3' region functional in the host cell may be substituted.

Two DNA sequences (such as a promoter region sequence and a sequence encoding a kinase of the invention) are said to be operably linked if the nature of the linkage between the two DNA sequences does not (1) result in the introduction of a frame-shift mutation, (2) interfere with the ability of the promoter region sequence to direct the transcription of a gene sequence encoding a kinase of the invention, or (3) interfere with the ability of the gene sequence of a kinase of the invention to be transcribed by the promoter region sequence. Thus, a promoter region would be operably linked to a DNA sequence if the promoter were capable of effecting transcription of that DNA sequence.

30

5

10

15

20

Thus, to express a gene encoding a kinase of the invention, transcriptional and translational signals recognized by an appropriate host are necessary.

The present invention encompasses the expression of a gene encoding a kinase of the invention (or a functional derivative thereof) in either prokaryotic or eukaryotic cells. Prokaryotic hosts are, generally, very efficient and convenient for the production of recombinant proteins and are, therefore, one type of preferred expression system for kinases of the invention. Prokaryotes most frequently are represented by various strains of *E. coli*. However, other microbial strains may also be used, including other bacterial strains.

10

5

In prokaryotic systems, plasmid vectors that contain replication sites and control sequences derived from a species compatible with the host may be used. Examples of suitable plasmid vectors may include pBR322, pUC118, pUC119 and the like; suitable phage or bacteriophage vectors may include  $\gamma$ gt10,  $\gamma$ gt11 and the like; and suitable virus vectors may include pMAM-neo, pKRC and the like. Preferably, the selected vector of the present invention has the capacity to replicate in the selected host cell.

15

Recognized prokaryotic hosts include bacteria such as E. coli, Bacillus, Streptomyces, Pseudomonas, Salmonella, Serratia, and the like. However, under such conditions, the polypeptide will not be glycosylated. The prokaryotic host must be compatible with the replicon and control sequences in the expression plasmid.

20

25

To express a kinase of the invention (or a functional derivative thereof) in a prokaryotic cell, it is necessary to operably link the sequence encoding the kinase of the invention to a functional prokaryotic promoter. Such promoters may be either constitutive or, more preferably, regulatable (*i.e.*, inducible or derepressible). Examples of constitutive promoters include the *int* promoter of bacteriophage  $\lambda$ , the *bla* promoter of the  $\beta$ -lactamase gene sequence of pBR322, and the *cat* promoter of the chloramphenicol acetyl transferase gene sequence of pPR325, and the like. Examples of inducible prokaryotic promoters include the major right and left promoters of bacteriophage  $\lambda$  ( $P_L$  and  $P_R$ ), the *trp, recA, \lambda acZ, \lambda acI,* and *gal* promoters of *E. coli*, the  $\alpha$ -amylase (Ulmanen *et al.*, J. Bacteriol. 162:176-182, 1985) and the  $\varsigma$ -28-specific promoters of *B. subtilis* (Gilman *et al.*, Gene Sequence 32:11-20, 1984), the promoters of the bacteriophages of *Bacillus* (Gryczan, In: The Molecular Biology of the Bacilli, Academic Press, Inc., NY, 1982), and *Streptomyces* promoters (Ward *et al.*, Mol. Gen. Genet. 203:468-478, 1986). Prokaryotic

WO 00/73469 PCT/US00/14842

83

promoters are reviewed by Glick (Ind. Microbiot. 1:277-282, 1987), Cenatiempo (Biochimie 68:505-516, 1986), and Gottesman (Ann. Rev. Genet. 18:415-442, 1984).

Proper expression in a prokaryotic cell also requires the presence of a ribosome-binding site upstream of the gene sequence-encoding sequence. Such ribosome-binding sites are disclosed, for example, by Gold *et al.* (Ann. Rev. Microbiol. 35:365-404, 1981). The selection of control sequences, expression vectors, transformation methods, and the like, are dependent on the type of host cell used to express the gene. As used herein, "cell", "cell line", and "cell culture" may be used interchangeably and all such designations include progeny. Thus, the words "transformants" or "transformed cells" include the primary subject cell and cultures derived therefrom, without regard to the number of transfers. It is also understood that all progeny may not be precisely identical in DNA content, due to deliberate or inadvertent mutations. However, as defined, mutant progeny have the same functionality as that of the originally transformed cell.

Host cells which may be used in the expression systems of the present invention are not strictly limited, provided that they are suitable for use in the expression of the kinase polypeptide of interest. Suitable hosts may often include eukaryotic cells. Preferred eukaryotic hosts include, for example, yeast, fungi, insect cells, mammalian cells either *in vivo*, or in tissue culture. Mammalian cells which may be useful as hosts include HeLa cells, cells of fibroblast origin such as VERO or CHO-K1, or cells of lymphoid origin and their derivatives. Preferred mammalian host cells include SP2/0 and J558L, as well as neuroblastoma cell lines such as IMR 332, which may provide better capacities for correct post-translational processing.

In addition, plant cells are also available as hosts, and control sequences compatible with plant cells are available, such as the cauliflower mosaic virus 35S and 19S, and nopaline synthase promoter and polyadenylation signal sequences. Another preferred host is an insect cell, for example the *Drosophila* larvae. Using insect cells as hosts, the *Drosophila* alcohol dehydrogenase promoter can be used (Rubin, Science 240:1453-1459, 1988). Alternatively, baculovirus vectors can be engineered to express large amounts of kinases of the invention in insect cells (Jasny, Science 238:1653, 1987; Miller *et al.*, In: Genetic Engineering, Vol. 8, Plenum, Setlow *et al.*, eds., pp. 277-297, 1986).

5

10

15

20

25

10

15

20

25

30

Any of a series of yeast expression systems can be utilized which incorporate promoter and termination elements from the actively expressed sequences coding for glycolytic enzymes that are produced in large quantities when yeast are grown in mediums rich in glucose. Known glycolytic gene sequences can also provide very efficient transcriptional control signals. Yeast provides substantial advantages in that it can also carry out post-translational modifications. A number of recombinant DNA strategies exist utilizing strong promoter sequences and high copy number plasmids which can be utilized for production of the desired proteins in yeast. Yeast recognizes leader sequences on cloned mammalian genes and secretes peptides bearing leader sequences (*i.e.*, prepeptides). Several possible vector systems are available for the expression of kinases of the invention in a mammalian host.

A wide variety of transcriptional and translational regulatory sequences may be employed, depending upon the nature of the host. The transcriptional and translational regulatory signals may be derived from viral sources, such as adenovirus, bovine papilloma virus, cytomegalovirus, simian virus, or the like, where the regulatory signals are associated with a particular gene sequence which has a high level of expression. Alternatively, promoters from mammalian expression products, such as actin, collagen, myosin, and the like, may be employed. Transcriptional initiation regulatory signals may be selected which allow for repression or activation, so that expression of the gene sequences can be modulated. Of interest are regulatory signals which are temperature-sensitive so that by varying the temperature, expression can be repressed or initiated, or are subject to chemical (such as metabolite) regulation.

Expression of kinases of the invention in eukaryotic hosts requires the use of eukaryotic regulatory regions. Such regions will, in general, include a promoter region sufficient to direct the initiation of RNA synthesis. Preferred eukaryotic promoters include, for example, the promoter of the mouse metallothionein I gene sequence (Hamer et al., J. Mol. Appl. Gen. 1:273-288, 1982); the TK promoter of Herpes virus (McKnight, Cell 31:355-365, 1982); the SV40 early promoter (Benoist et al., Nature (London) 290:304-31, 1981); and the yeast gal4 gene sequence promoter (Johnston et al., Proc. Natl. Acad. Sci. (USA) 79:6971-6975, 1982; Silver et al., Proc. Natl. Acad. Sci. (USA) 81:5951-5955, 1984).

10

15

20

25

30

Translation of eukaryotic mRNA is initiated at the codon that encodes the first methionine. For this reason, it is preferable to ensure that the linkage between a eukaryotic promoter and a DNA sequence which encodes a kinase of the invention (or a functional derivative thereof) does not contain any intervening codons which are capable of encoding a methionine (i.e., AUG). The presence of such codons results either in the formation of a fusion protein (if the AUG codon is in the same reading frame as the kinase of the invention coding sequence) or a frame-shift mutation (if the AUG codon is not in the same reading frame as the kinase of the invention coding sequence).

A nucleic acid molecule encoding a kinase of the invention and an operably linked promoter may be introduced into a recipient prokaryotic or eukaryotic cell either as a nonreplicating DNA or RNA molecule, which may either be a linear molecule or, more preferably, a closed covalent circular molecule. Since such molecules are incapable of autonomous replication, the expression of the gene may occur through the transient expression of the introduced sequence. Alternatively, permanent expression may occur through the integration of the introduced DNA sequence into the host chromosome.

A vector may be employed which is capable of integrating the desired gene sequences into the host cell chromosome. Cells which have stably integrated the introduced DNA into their chromosomes can be selected by also introducing one or more markers which allow for selection of host cells which contain the expression vector. The marker may provide for prototrophy to an auxotrophic host, biocide resistance, *e.g.*, antibiotics, or heavy metals, such as copper, or the like. The selectable marker gene sequence can either be directly linked to the DNA gene sequences to be expressed, or introduced into the same cell by co-transfection. Additional elements may also be needed for optimal synthesis of mRNA. These elements may include splice signals, as well as transcription promoters, enhancers, and termination signals. cDNA expression vectors incorporating such elements include those described by Okayama (Mol. Cell. Biol. 3:280-, 1983).

The introduced nucleic acid molecule can be incorporated into a plasmid or viral vector capable of autonomous replication in the recipient host. Any of a wide variety of vectors may be employed for this purpose. Factors of importance in selecting a particular plasmid or viral vector include: the ease with which recipient cells that contain the vector may be recognized and selected from those recipient cells which do not contain the vector;

BNSDOCID: <WO

0073469A2 I >

10

15

20

25

30

the number of copies of the vector which are desired in a particular host; and whether it is desirable to be able to "shuttle" the vector between host cells of different species.

Preferred prokaryotic vectors include plasmids such as those capable of replication in *E. coli* (such as, for example, pBR322, ColEl, pSC101, pACYC 184, πVX; "Molecular Cloning: A Laboratory Manual", 1989, *supra*). Bacillus plasmids include pC194, pC221, pT127, and the like (Gryczan, In: The Molecular Biology of the Bacilli, Academic Press, NY, pp. 307-329, 1982). Suitable *Streptomyces* plasmids include p1J101 (Kendall *et al.*, J. Bacteriol. 169:4177-4183, 1987), and streptomyces bacteriophages such as φC31 (Chater *et al.*, In: Sixth International Symposium on Actinomycetales Biology, Akademiai Kaido, Budapest, Hungary, pp. 45-54, 1986). *Pseudomonas* plasmids are reviewed by John *et al.* (Rev. Infect. Dis. 8:693-704, 1986), and Izaki (Jpn. J. Bacteriol. 33:729-742, 1978).

Preferred eukaryotic plasmids include, for example, BPV, vaccinia, SV40, 2-micron circle, and the like, or their derivatives. Such plasmids are well known in the art (Botstein *et al.*, Miami Wntr. Symp. 19:265-274, 1982; Broach, In: "The Molecular Biology of the Yeast Saccharomyces: Life Cycle and Inheritance", Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, p. 445-470, 1981; Broach, Cell 28:203-204, 1982; Bollon *et al.*, J. Clin. Hematol. Oncol. 10:39-48, 1980; Maniatis, In: Cell Biology: A Comprehensive Treatise, Vol. 3, Gene Sequence Expression, Academic Press, NY, pp. 563-608, 1980).

Once the vector or nucleic acid molecule containing the construct(s) has been prepared for expression, the DNA construct(s) may be introduced into an appropriate host cell by any of a variety of suitable means, i.e., transformation, transfection, conjugation, protoplast fusion, electroporation, particle gun technology, calcium phosphate-precipitation, direct microinjection, and the like. After the introduction of the vector, recipient cells are grown in a selective medium, which selects for the growth of vector-containing cells. Expression of the cloned gene(s) results in the production of a kinase of the invention, or fragments thereof. This can take place in the transformed cells as such, or following the induction of these cells to differentiate (for example, by administration of bromodeoxyuracil to neuroblastoma cells or the like). A variety of incubation conditions can be used to form the peptide of the present invention. The most preferred conditions are those which mimic physiological conditions.

### IV. The Proteins of the Invention

A variety of methodologies known in the art can be utilized to obtain the polypeptides of the present invention. The polypeptides may be purified from tissues or cells that naturally produce the polypeptides. Alternatively, the above-described isolated nucleic acid fragments could be used to express the kinases of the invention in any organism. The samples of the present invention include cells, protein extracts or membrane extracts of cells, or biological fluids. The samples will vary based on the assay format, the detection method, and the nature of the tissues, cells or extracts used as the sample.

10

5

Any eukaryotic organism can be used as a source for the polypeptides of the invention, as long as the source organism naturally contains such polypeptides. As used herein, "source organism" refers to the original organism from which the amino acid sequence of the subunit is derived, regardless of the organism the subunit is expressed in and ultimately isolated from.

15

One skilled in the art can readily follow known methods for isolating proteins in order to obtain the polypeptides free of natural contaminants. These include, but are not limited to: size-exclusion chromatography, HPLC, ion-exchange chromatography, and immuno-affinity chromatography.

20

25

30

Further, the polypeptides of the invention include the full-length polypeptides that can be identified from the full-length or partial sequences encoded by SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182,

10

15

20

25

30

SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242 (Figure 1). In addition, the polypeptides of the invention include the domains of these polypeptides, including, but not limited to, the N-terminal, kinase/catalytic, and C-terminal domains.

The characteristics of the protein kinase nucleic acid sequences of the invention are provided in Table 1. The protein kinases fall into 10 known groups: AGC, CAMK, CKI, CMGC, dsPK, EIFK, LIMK, MLK, STE and TK. In addition, there are a significant number of protein kinases that do not belong to any of the known groups, and therefore presumably define new protein kinase groups.

Additional characteristics are shown in, *inter alia*, the tables, namely Table 1, Table 2, Table 3 and Table 4, provided below.

# V. <u>Antibodies, Hybridomas, Methods of Use and Kits for Detection of Protein</u> Kinases

The present invention relates to an antibody having binding affinity to a kinase of the invention. The polypeptide may have an amino acid sequence selected from the group consisting of those set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ

10

15

20

25

30

ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or a functional derivative thereof, or at least 9 contiguous amino acids thereof (preferably, at least 20, 30, 35, or 40 or more contiguous amino acids thereof). Alternatively, the antibody may bind to a part of the polypeptide not provided in the sequences above, but that is present in the full-length sequence of the polypeptide and that is easily obtained using methods standard in the art. Further, the antibody may bind specifically to particular domains of one or more of the kinases of the invention, including, but not limited to, the N-terminal, kinase/catalytic, or C-terminal domains.

The present invention also relates to an antibody having specific binding affinity to a kinase or kinase domain of the invention. Such an antibody may be isolated by comparing its binding affinity to a kinase of the invention with its binding affinity to other polypeptides. Those that bind selectively to a kinase of the invention would be chosen for use in methods requiring a distinction between a kinase of the invention and other

10

15

20

25

polypeptides. Such methods could include, but should not be limited to, the analysis of altered kinase expression in tissue containing other polypeptides.

The kinases of the present invention can be used in a variety of procedures and methods, such as for the generation of antibodies, for use in identifying pharmaceutical compositions, and for studying DNA/protein interaction.

The kinases of the present invention can be used to produce antibodies or hybridomas. One skilled in the art will recognize that if an antibody is desired, such a peptide could be generated as described herein and used as an immunogen. The antibodies of the present invention include monoclonal and polyclonal antibodies, as well fragments of these antibodies, and humanized forms. Humanized forms of the antibodies of the present invention may be generated using one of the procedures known in the art such as chimerization or CDR grafting.

The present invention also relates to a hybridoma that produces the abovedescribed monoclonal antibody, or binding fragment thereof. A hybridoma is an immortalized cell line that is capable of secreting a specific monoclonal antibody.

In general, techniques for preparing monoclonal antibodies and hybridomas are well known in the art (Campbell, "Monoclonal Antibody Technology: Laboratory Techniques in Biochemistry and Molecular Biology," Elsevier Science Publishers, Amsterdam, The Netherlands, 1984; St. Groth *et al.*, J. Immunol. Methods 35:1-21, 1980). Any animal (mouse, rabbit, and the like) which is known to produce antibodies can be immunized with the selected polypeptide. Methods for immunization are well known in the art. Such methods include subcutaneous or intraperitoneal injection of the polypeptide. One skilled in the art will recognize that the amount of polypeptide used for immunization will vary based on the animal that is immunized, the antigenicity of the polypeptide and the site of injection.

The polypeptide may be modified or administered in an adjuvant in order to increase the peptide antigenicity. Methods of increasing the antigenicity of a polypeptide are well known in the art. Such procedures include coupling the antigen with a heterologous protein (such as globulin or  $\beta$ -galactosidase) or through the inclusion of an adjuvant during immunization.

10

15

20

25

30

For monoclonal antibodies, spleen cells from the immunized animals are removed, fused with myeloma cells, such as SP2/0-Agl4 myeloma cells, and allowed to become monoclonal antibody producing hybridoma cells. Any one of a number of methods well known in the art can be used to identify the hybridoma cell that produces an antibody with the desired characteristics. These include screening the hybridomas with an ELISA assay, western blot analysis, or radioimmunoassay (Lutz et al., Exp. Cell Res. 175:109-124, 1988). Hybridomas secreting the desired antibodies are cloned and the class and subclass are determined using procedures known in the art (Campbell, "Monoclonal Antibody Technology: Laboratory Techniques in Biochemistry and Molecular Biology", supra, 1984).

For polyclonal antibodies, antibody-containing antisera is isolated from the immunized animal and is screened for the presence of antibodies with the desired specificity using one of the above-described procedures. The above-described antibodies may be detectably labeled. Antibodies can be detectably labeled through the use of radioisotopes, affinity labels (such as biotin, avidin, and the like), enzymatic labels (such as horse radish peroxidase, alkaline phosphatase, and the like) fluorescent labels (such as FITC or rhodamine, and the like), paramagnetic atoms, and the like. Procedures for accomplishing such labeling are well-known in the art, for example, see Stemberger et al., J. Histochem. Cytochem. 18:315, 1970; Bayer et al., Meth. Enzym. 62:308-, 1979; Engval et al., Immunol. 109:129-, 1972; Goding, J. Immunol. Meth. 13:215-, 1976. The labeled antibodies of the present invention can be used for in vitro, in vivo, and in situ assays to identify cells or tissues that express a specific peptide.

The above-described antibodies may also be immobilized on a solid support. Examples of such solid supports include plastics such as polycarbonate, complex carbohydrates such as agarose and sepharose, acrylic resins and such as polyacrylamide and latex beads. Techniques for coupling antibodies to such solid supports are well known in the art (Weir et al., "Handbook of Experimental Immunology" 4th Ed., Blackwell Scientific Publications, Oxford, England, Chapter 10, 1986; Jacoby et al., Meth. Enzym. 34, Academic Press, N.Y., 1974). The immobilized antibodies of the present invention can be used for in vitro, in vivo, and in situ assays as well as in immunochromotography.

10

15

20

25

30

Furthermore, one skilled in the art can readily adapt currently available procedures, as well as the techniques, methods and kits disclosed herein with regard to antibodies, to generate peptides capable of binding to a specific peptide sequence in order to generate rationally designed antipeptide peptides (Hurby et al., "Application of Synthetic Peptides: Antisense Peptides", In Synthetic Peptides, A User's Guide, W.H. Freeman, NY, pp. 289-307, 1992; Kaspczak et al., Biochemistry 28:9230-9238, 1989).

Anti-peptide peptides can be generated by replacing the basic amino acid residues found in the peptide sequences of the kinases of the invention with acidic residues, while maintaining hydrophobic and uncharged polar groups. For example, lysine, arginine, and/or histidine residues are replaced with aspartic acid or glutamic acid and glutamic acid residues are replaced by lysine, arginine or histidine.

The present invention also encompasses a method of detecting a kinase polypeptide in a sample, comprising: (a) contacting the sample with an above-described antibody, under conditions such that immunocomplexes form, and (b) detecting the presence of said antibody bound to the polypeptide. In detail, the methods comprise incubating a test sample with one or more of the antibodies of the present invention and assaying whether the antibody binds to the test sample. Altered levels of a kinase of the invention in a sample as compared to normal levels may indicate disease.

Conditions for incubating an antibody with a test sample vary. Incubation conditions depend on the format employed in the assay, the detection methods employed, and the type and nature of the antibody used in the assay. One skilled in the art will recognize that any one of the commonly available immunological assay formats (such as radioimmunoassays, enzyme-linked immunosorbent assays, diffusion based Ouchterlony, or rocket immunofluorescent assays) can readily be adapted to employ the antibodies of the present invention. Examples of such assays can be found in Chard ("An Introduction to Radioimmunoassay and Related Techniques" Elsevier Science Publishers, Amsterdam, The Netherlands, 1986), Bullock *et al.* ("Techniques in Immunocytochemistry," Academic Press, Orlando, FL Vol. 1, 1982; Vol. 2, 1983; Vol. 3, 1985), Tijssen ("Practice and Theory of Enzyme Immunoassays: Laboratory Techniques in Biochemistry and Molecular Biology," Elsevier Science Publishers, Amsterdam, The Netherlands, 1985).

BNSDOCID: <WO\_\_\_\_\_0073469A2\_1\_>

The immunological assay test samples of the present invention include cells, protein or membrane extracts of cells, or biological fluids such as blood, serum, plasma, or urine. The test samples used in the above-described method will vary based on the assay format, nature of the detection method and the tissues, cells or extracts used as the sample to be assayed. Methods for preparing protein extracts or membrane extracts of cells are well known in the art and can be readily be adapted in order to obtain a sample which is testable with the system utilized.

A kit contains all the necessary reagents to carry out the previously described methods of detection. The kit may comprise: (i) a first container means containing an above-described antibody, and (ii) second container means containing a conjugate comprising a binding partner of the antibody and a label. In another preferred embodiment, the kit further comprises one or more other containers comprising one or more of the following: wash reagents and reagents capable of detecting the presence of bound antibodies.

Examples of detection reagents include, but are not limited to, labeled secondary antibodies, or in the alternative, if the primary antibody is labeled, the chromophoric, enzymatic, or antibody binding reagents that are capable of reacting with the labeled antibody. The compartmentalized kit may be as described above for nucleic acid probe kits. One skilled in the art will readily recognize that the antibodies described in the present invention can readily be incorporated into one of the established kit formats that are well known in the art.

# VI. Isolation of Compounds That Interact With Protein Kinases

The present invention also relates to a method of detecting a compound capable of binding to a protein kinase of the invention, comprising incubating the compound with a kinase of the invention and detecting the presence of the compound bound to the kinase. The compound may be present within a complex mixture, for example, serum, body fluid, or cell extracts.

The present invention also relates to a method of detecting an agonist or antagonist of kinase activity or kinase binding partner activity comprising incubating cells that produce a kinase of the invention in the presence of a compound and detecting changes in the level of kinase activity or kinase binding partner activity. The compounds thus identified would produce a change in activity indicative of the presence of the compound.

15

5

10

20

30

The compound may be present within a complex mixture, for example, serum, body fluid, or cell extracts. Once the compound is identified it can be isolated using techniques well known in the art.

The present invention also encompasses a method of agonizing (stimulating) or antagonizing kinase associated activity in a mammal comprising administering to said mammal an agonist or antagonist to a kinase of the invention in an amount sufficient to effect said agonism or antagonism. A method of treating diseases in a mammal with an agonist or antagonist of kinase activity comprising administering the agonist or antagonist to a mammal in an amount sufficient to agonize or antagonize kinase associated functions is also encompassed in the present application.

In an effort to discover novel treatments for diseases, biomedical researchers and chemists have designed, synthesized, and tested molecules that inhibit the function of protein kinases. Some small organic molecules form a class of compounds that modulate the function of protein kinases. Examples of molecules that have been reported to inhibit the function of protein kinases include, but are not limited to, bis monocyclic, bicyclic or heterocyclic aryl compounds (PCT WO 92/20642, published November 26, 1992 by Maguire et al.), vinylene-azaindole derivatives (PCT WO 94/14808, published July 7, 1994 by Ballinari et al.), 1-cyclopropyl-4-pyridyl-quinolones (U.S. Patent No. 5,330,992), styryl compounds (U.S. Patent No. 5,217,999), styryl-substituted pyridyl compounds (U.S. Patent No. 5,302,606), certain quinazoline derivatives (EP Application No. 0 566 266 A1), seleoindoles and selenides (PCT WO 94/03427, published February 17, 1994 by Denny et al.), tricyclic polyhydroxylic compounds (PCT WO 92/21660, published December 10, 1992 by Dow), and benzylphosphonic acid compounds (PCT WO 91/15495, published October 17, 1991 by Dow et al).

Compounds that can traverse cell membranes and are resistant to acid hydrolysis are potentially advantageous as therapeutics as they can become highly bioavailable after being administered orally to patients. However, many of these protein kinase inhibitors only weakly inhibit the function of protein kinases. In addition, many inhibit a variety of protein kinases and will cause multiple side-effects as therapeutics for diseases.

Some indolinone compounds, however, form classes of acid resistant and membrane permeable organic molecules. WO 96/22976 (published August 1, 1996 by Ballinari et al.) describes hydrosoluble indolinone compounds that harbor tetralin,

10

5

20

15

25

30

BNSDOCID: <WO 0073469A2 | >

10

15

20

25

30

naphthalene, quinoline, and indole substituents fused to the oxindole ring. These bicyclic substituents are in turn substituted with polar moieties including hydroxylated alkyl, phosphate, and ether moieties. U.S. Patent Application Serial Nos. 08/702,232, filed August 23, 1996, entitled "Indolinone Combinatorial Libraries and Related Products and Methods for the Treatment of Disease" by Tang et al. (Lyon & Lyon Docket No. 221/187) and 08/485,323, filed June 7, 1995, entitled "Benzylidene-Z-Indoline Compounds for the Treatment of Disease" by Tang et al. (Lyon & Lyon Docket No. 223/298) and International Patent Publication WO 96/22976, published August 1, 1996 by Ballinari et al., all of which are incorporated herein by reference in their entirety, including any drawings, describe indolinone chemical libraries of indolinone compounds harboring other bicyclic moieties as well as monocyclic moieties fused to the oxindole ring. Applications 08/702,232, filed August 23, 1996, entitled "Indolinone Combinatorial Libraries and Related Products and Methods for the Treatment of Disease" by Tang et al. (Lyon & Lyon Docket No. 221/187), 08/485,323, filed June 7, 1995, entitled "Benzylidene-Z-Indoline Compounds for the Treatment of Disease" by Tang et al. (Lyon & Lyon Docket No. 223/298), and WO 96/22976, published August 1, 1996 by Ballinari et al. teach methods of indolinone synthesis, methods of testing the biological activity of indolinone compounds in cells, and inhibition patterns of indolinone derivatives.

Other examples of substances capable of modulating kinase activity include, but are not limited to, tyrphostins, quinazolines, quinoxolines, and quinolines. The quinazolines, tyrphostins, quinolines, and quinoxolines referred to above include well known compounds such as those described in the literature. For example, representative publications describing quinazolines include Barker *et al.*, EPO Publication No. 0 520 722 A1; Jones *et al.*, U.S. Patent No.4,447,608; Kabbe *et al.*, U.S. Patent No. 4,757,072; Kaul and Vougioukas, U.S. Patent No. 5, 316,553; Kreighbaum and Comer, U.S. Patent No. 4,343,940; Pegg and Wardleworth, EPO Publication No. 0 562 734 A1; Barker *et al.*, Proc. of Am. Assoc. for Cancer Research 32:327 (1991); Bertino, J.R., Cancer Research 3:293-304 (1979); Bertino, J.R., Cancer Research 9(2 part 1):293-304 (1979); Curtin *et al.*, Br. J. Cancer 53:361-368 (1986); Fernandes *et al.*, Cancer Research 43:1117-1123 (1983); Ferris *et al.* J. Org. Chem. 44(2):173-178; Fry *et al.*, Science 265:1093-1095 (1994); Jackman *et al.*, Cancer Research 51:5579-5586 (1981); Jones *et al.* J. Med. Chem. 29(6):1114-1118; Lee and Skibo, Biochemistry 26(23):7355-7362 (1987); Lemus *et al.*, J.

10

15

20

25

30

Org. Chem. 54:3511-3518 (1989); Ley and Seng, Synthesis 1975:415-522 (1975); Maxwell et al., Magnetic Resonance in Medicine 17:189-196 (1991); Mini et al., Cancer Research 45:325-330 (1985); Phillips and Castle, J. Heterocyclic Chem. 17(19):1489-1596 (1980); Reece et al., Cancer Research 47(11):2996-2999 (1977); Sculier et al., Cancer Immunol. and Immunother. 23:A65 (1986); Sikora et al., Cancer Letters 23:289-295 (1984); Sikora et al., Analytical Biochem. 172:344-355 (1988); all of which are incorporated herein by reference in their entirety, including any drawings.

Quinoxaline is described in Kaul and Vougioukas, U.S. Patent No. 5,316,553, incorporated herein by reference in its entirety, including any drawings.

Quinolines are described in Dolle et al., J. Med. Chem. 37:2627-2629 (1994); MaGuire, J. Med. Chem. 37:2129-2131 (1994); Burke et al., J. Med. Chem. 36:425-432 (1993); and Burke et al. BioOrganic Med. Chem. Letters 2:1771-1774 (1992), all of which are incorporated by reference in their entirety, including any drawings.

Tyrphostins are described in Allen et al., Clin. Exp. Immunol. 91:141-156 (1993); Anafi et al., Blood 82:12:3524-3529 (1993), Baker et al., J. Cell Sci. 102:543-555 (1992); Bilder et al., Amer. Physiol. Soc. pp. 6363-6143:C721-C730 (1991); Brunton et al., Proceedings of Amer. Assoc. Cancer Rsch. 33:558 (1992); Bryckaert et al., Experimental Cell Research 199:255-261 (1992); Dong et al., J. Leukocyte Biology 53:53-60 (1993); Dong et al., J. Immunol. 151(5):2717-2724 (1993); Gazit et al., J. Med. Chem. 32:2344-2352 (1989); Gazit et al., "J. Med. Chem. 36:3556-3564 (1993); Kaur et al., Anti-Cancer Drugs 5:213-222 (1994); Kaur et al., King et al., Biochem. J. 275:413-418 (1991); Kuo et al., Cancer Letters 74:197-202 (1993); Levitzki, A., The FASEB J. 6:3275-3282 (1992); Lyall et al., J. Biol. Chem. 264:14503-14509 (1989); Peterson et al., The Prostate 22:335-345 (1993); Pillemer et al., Int. J. Cancer 50:80-85 (1992); Posner et al., Molecular Pharmacology 45:673-683 (1993); Rendu et al., Biol. Pharmacology 44(5):881-888 (1992); Sauro and Thomas, Life Sciences 53:371-376 (1993); Sauro and Thomas, J. Pharm. and Experimental Therapeutics 267(3):119-1125 (1993); Wolbring et al., J. Biol. Chem. 269(36):22470-22472 (1994); and Yoneda et al., Cancer Research 51:4430-4435 (1991); all of which are incorporated herein by reference in their entirety, including any drawings.

10

15

20

25

Other compounds that could be used as modulators include oxindolinones such as those described in U.S. patent application Serial No. 08/702,232 filed August 23, 1996, incorporated herein by reference in its entirety, including any drawings.

# VII. <u>Biological Significance</u>, Applications and Clinical Relevance of Novel Protein Kinases

For each protein kinase in this application, we provide a classification of the protein class and family to which it belongs, a summary of non-cataltyic protein motifs, a profile of its expression in several hundred tissue and cell sources, and a chromosomal location. This information can be used to suggest potential function, regulation or therapeutic utility for each of the proteins.

The kinase classification and protein domains often reflect pathways, cellular roles, or mechanisms of up- or down-stream regulation. Also disease-relevant genes often occur in families of related genes. For example if one member of a kinase family functions as an oncogene, a tumor suppressor, or has been found to be disrupted in an immune, neurologic, cardiovascular, or metabolic disorder, frequently other family members may play a related role.

The expression analysis organizes kinases into groups that are transcriptionally upregulated in tumors and those that are more restricted to specific tumor types such as melanoma or prostate. This analysis also identifies genes that are regulated in a cell cycle dependent manner, and are therefore likely to be involved in maintaining cell cycle checkpoints, entry, progression, or exit from mitosis, oversee DNA repair, or are involved in cell proliferation and genome stability. Expression data also can identify genes expressed in endothelial sources or other tissues that suggest a role in angiogenesis, thereby implicating them as targets for control of diseases that have an angiogenic component, such as cancer, endometriosis, retinopathy and macular degeneration, and various ischemic or vascular pathologies. A proteins' role in cell survival can also be suggested based on restricted expression in cells subjected to external stress such as oxidative damage, hypoxia, drugs such as cisplatinum, or irradiation. Metastases-associated genes can be implicated when expression is restricted to invading regions of a tumor, or is only seen in local or distant metastases compared to the primary tumor, or when a gene is upregulated during cell culture models of invasion, migration, or motility.

Chromosomal location can identify candidate targets for a tumor amplicon or a tumor-suppressor locus. Summaries of prevelant tumor amplicons are available in the literature, and can identify tumor types to experimentally be confirmed to contain amplified copies of a kinase gene which localizes to an adjacent region.

5

11

Based on these criteria several kinases immediately stand out as being of potential therapeutic relevance. The protein kinases can be divided into the following disease-relevant categories (nucleotide Seq ID #s in parentheses):

Tumor associated: Mok (SEQ ID NO:NO:57), EPK2, AA316804 (SEQ ID NO:11), AA435956 (SEQ ID NO:NO:48), AA278842 (SEQ ID NO:88), AA599286 (SEQ ID NO:89), AA826850 (SEQ ID NO:3), HRI (SEQ ID NO:73), MLK4 AA232253 (SEQ ID NO:82), AA883975 SGK 235 (SEQ ID NO:95), AA311714 (SEQ ID NO:101), MPSK1 (SEQ ID NO:110), R19609 (Seq ID111), AA383293 (SEQ ID NO:26).

Prostate-specific: AA234451 (SEQ ID NO:47), TSK4 (SEQ ID NO:93), RIP4 (SEQ ID NO:84), KIAA0965 (SEQ ID NO:8).

15

20

25

30

10

Oncogenic or proliferation associated: KIAA0781 (SEQ ID NO:38), AA789239 (SEQ ID NO:52), CCRK (SEQ ID NO:54), CLK4 (SEQ ID NO:55), H85389 (SEQ ID NO:97).

Neuronal restricted: CAMKKB (SEQ ID NO:66)

Hematopoietic expressed: PTK9L (SEQ ID NO:22), DRAK2 (SEQ ID NO:29), AI025291 (SEQ ID NO:94)

Angiogenic or endothelial expressed: DRAK1 (SEQ ID NO:31), MAK-V (SEQ ID NO:40), TRAD (SEQ ID NO:44), MOK (SEQ ID NO:57), AA08847 (SEQ ID NO:78), HGP\_66444466 (SEQ ID NO:79), RSK4 (SEQ ID NO:16).

Cell cycle regulated: AA454060 (SEQ ID NO:45), KIAA0999 (Mitotic – SEQ ID NO:32), AA579641 (Mitotic – SEQ ID NO:60), AA305176 (Mitotic – SEQ ID NO:6), AA018361 (S1 phase – SEQ ID NO:100).

### VIII. Transgenic Animals.

A variety of methods are available for the production of transgenic animals associated with this invention. DNA can be injected into the pronucleus of a fertilized egg before fusion of the male and female pronuclei, or injected into the nucleus of an embryonic cell (e.g., the nucleus of a two-cell embryo) following the initiation of cell division (Brinster et al., Proc. Nat. Acad. Sci. USA 82: 4438-4442, 1985). Embryos can

be infected with viruses, especially retroviruses, modified to carry inorganic-ion receptor nucleotide sequences of the invention.

Pluripotent stem cells derived from the inner cell mass of the embryo and stabilized in culture can be manipulated in culture to incorporate nucleotide sequences of the invention. A transgenic animal can be produced from such cells through implantation into a blastocyst that is implanted into a foster mother and allowed to come to term. Animals suitable for transgenic experiments can be obtained from standard commercial sources such as Charles River (Wilmington, MA), Taconic (Germantown, NY), Harlan Sprague Dawley (Indianapolis, IN), etc.

The procedures for manipulation of the rodent embryo and for microinjection of DNA into the pronucleus of the zygote are well known to those of ordinary skill in the art (Hogan et al., supra). Microinjection procedures for fish, amphibian eggs and birds are detailed in Houdebine and Chourrout (Experientia 47: 897-905, 1991). Other procedures for introduction of DNA into tissues of animals are described in U.S. Patent No., 4,945,050 (Sanford et al., July 30, 1990).

By way of example only, to prepare a transgenic mouse, female mice are induced to superovulate. Females are placed with males, and the mated females are sacrificed by CO<sub>2</sub> asphyxiation or cervical dislocation and embryos are recovered from excised oviducts. Surrounding cumulus cells are removed. Pronuclear embryos are then washed and stored until the time of injection. Randomly cycling adult female mice are paired with vasectomized males. Recipient females are mated at the same time as donor females. Embryos then are transferred surgically. The procedure for generating transgenic rats is similar to that of mice (Hammer et al., Cell 63:1099-1112, 1990).

Methods for the culturing of embryonic stem (ES) cells and the subsequent production of transgenic animals by the introduction of DNA into ES cells using methods such as electroporation, calcium phosphate/DNA precipitation and direct injection also are well known to those of ordinary skill in the art (Teratocarcinomas and Embryonic Stem Cells, A Practical Approach, E.J. Robertson, ed., IRL Press, 1987).

In cases involving random gene integration, a clone containing the sequence(s) of the invention is co-transfected with a gene encoding resistance. Alternatively, the gene encoding neomycin resistance is physically linked to the sequence(s) of the invention.

15

10

5

20

25

Ġ

5

10

15

20

25

30

Transfection and isolation of desired clones are carried out by any one of several methods well known to those of ordinary skill in the art (E.J. Robertson, *supra*).

DNA molecules introduced into ES cells can also be integrated into the chromosome through the process of homologous recombination (Capecchi, Science 244: 1288-1292, 1989). Methods for positive selection of the recombination event (i.e., neo resistance) and dual positive-negative selection (i.e., neo resistance and gancyclovir resistance) and the subsequent identification of the desired clones by PCR have been described by Capecchi, supra and Joyner et al. (Nature 338: 153-156, 1989), the teachings of which are incorporated herein in their entirety including any drawings. The final phase of the procedure is to inject targeted ES cells into blastocysts and to transfer the blastocysts into pseudopregnant females. The resulting chimeric animals are bred and the offspring are analyzed by Southern blotting to identify individuals that carry the transgene. Procedures for the production of non-rodent mammals and other animals have been discussed by others (Houdebine and Chourrout, supra; Pursel et al., Science 244:1281-1288, 1989; and Simms et al., Bio/Technology 6:179-183, 1988).

Thus, the invention provides transgenic, nonhuman mammals containing a transgene encoding a kinase of the invention or a gene effecting the expression of the kinase. Such transgenic nonhuman mammals are particularly useful as an *in vivo* test system for studying the effects of introduction of a kinase, or regulating the expression of a kinase (*i.e.*, through the introduction of additional genes, antisense nucleic acids, or ribozymes).

A "transgenic animal" is an animal having cells that contain DNA which has been artificially inserted into a cell, which DNA becomes part of the genome of the animal which develops from that cell. Preferred transgenic animals are primates, mice, rats, cows, pigs, horses, goats, sheep, dogs and cats. The transgenic DNA may encode human STE20-related kinases. Native expression in an animal may be reduced by providing an amount of anti-sense RNA or DNA effective to reduce expression of the receptor.

## IX. Gene Therapy

Protein kinases of the invention, or their genetic sequences will also be useful in gene therapy (reviewed in Miller, Nature 357:455-460, 1992). Miller states that advances have resulted in practical approaches to human gene therapy that have demonstrated

BNSDCCID: <WO\_\_\_\_\_0073469A2\_I\_>

positive initial results. The basic science of gene therapy is described in Mulligan (Science 260:926-931, 1993).

In one preferred embodiment, an expression vector containing protein kinase coding sequence is inserted into cells, the cells are grown *in vitro*, and then are infused in large numbers into patients. In another preferred embodiment, a DNA segment containing a promoter of choice (for example a strong promoter) is transferred into cells containing an endogenous gene encoding kinases of the invention in such a manner that the promoter segment enhances expression of the endogenous kinase gene (for example, the promoter segment is transferred to the cell such that it becomes directly linked to the endogenous kinase gene).

The gene therapy may involve the use of an adenovirus containing kinase cDNA targeted to a tumor, systemic kinase increase by implantation of engineered cells, injection with kinase-encoding virus, or injection of naked kinase DNA into appropriate tissues.

Target cell populations may be modified by introducing altered forms of one or more components of the protein complexes in order to modulate the activity of such complexes. For example, by reducing or inhibiting a complex component activity within target cells, an abnormal signal transduction event(s) leading to a condition may be decreased, inhibited, or reversed. Deletion or missense mutants of a component, that retain the ability to interact with other components of the protein complexes but cannot function in signal transduction may be used to inhibit an abnormal, deleterious signal transduction event.

Expression vectors derived from viruses such as retroviruses, vaccinia virus, adenovirus, adeno-associated virus, herpes viruses, several RNA viruses, or bovine papilloma virus, may be used for delivery of nucleotide sequences (e.g., cDNA) encoding recombinant kinase of the invention protein into the targeted cell population (e.g., tumor cells). Methods which are well known to those skilled in the art can be used to construct recombinant viral vectors containing coding sequences (Maniatis et al., Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, N.Y., 1989; Ausubel et al., Current Protocols in Molecular Biology, Greene Publishing Associates and Wiley Interscience, N.Y., 1989). Alternatively, recombinant nucleic acid molecules encoding protein sequences can be used as naked DNA or in a reconstituted system e.g., liposomes or other lipid systems for delivery to target cells (e.g., Felgner et al., Nature 337:387-8,

5

10

15

20

25

5

10

15

20

25

30

1989). Several other methods for the direct transfer of plasmid DNA into cells exist for use in human gene therapy and involve targeting the DNA to receptors on cells by complexing the plasmid DNA to proteins (Miller, supra).

In its simplest form, gene transfer can be performed by simply injecting minute amounts of DNA into the nucleus of a cell, through a process of microinjection (Capecchi, Cell 22:479-88, 1980). Once recombinant genes are introduced into a cell, they can be recognized by the cell's normal mechanisms for transcription and translation, and a gene product will be expressed. Other methods have also been attempted for introducing DNA into larger numbers of cells. These methods include: transfection, wherein DNA is precipitated with CaPO<sub>4</sub> and taken into cells by pinocytosis (Chen *et al.*, Mol. Cell Biol. 7:2745-52, 1987); electroporation, wherein cells are exposed to large voltage pulses to introduce holes into the membrane (Chu *et al.*, Nucleic Acids Res. 15:1311-26, 1987); lipofection/liposome fusion, wherein DNA is packaged into lipophilic vesicles which fuse with a target cell (Felgner *et al.*, Proc. Natl. Acad. Sci. USA. 84:7413-7417, 1987); and particle bombardment using DNA bound to small projectiles (Yang *et al.*, Proc. Natl. Acad. Sci. 87:9568-9572, 1990). Another method for introducing DNA into cells is to couple the DNA to chemically modified proteins.

It has also been shown that adenovirus proteins are capable of destabilizing endosomes and enhancing the uptake of DNA into cells. The admixture of adenovirus to solutions containing DNA complexes, or the binding of DNA to polylysine covalently attached to adenovirus using protein crosslinking agents substantially improves the uptake and expression of the recombinant gene (Curiel *et al.*, Am. J. Respir. Cell. Mol. Biol., 6:247-52, 1992).

As used herein "gene transfer" means the process of introducing a foreign nucleic acid molecule into a cell. Gene transfer is commonly performed to enable the expression of a particular product encoded by the gene. The product may include a protein, polypeptide, anti-sense DNA or RNA, or enzymatically active RNA. Gene transfer can be performed in cultured cells or by direct administration into animals. Generally gene transfer involves the process of nucleic acid contact with a target cell by non-specific or receptor mediated interactions, uptake of nucleic acid into the cell through the membrane or by endocytosis, and release of nucleic acid into the cytoplasm from the plasma membrane or endosome. Expression may require, in addition, movement of the nucleic

10

15

20

25

30

acid into the nucleus of the cell and binding to appropriate nuclear factors for transcription.

As used herein "gene therapy" is a form of gene transfer and is included within the definition of gene transfer as used herein and specifically refers to gene transfer to express a therapeutic product from a cell in vivo or in vitro. Gene transfer can be performed ex vivo on cells which are then transplanted into a patient, or can be performed by direct administration of the nucleic acid or nucleic acid-protein complex into the patient.

In another preferred embodiment, a vector having nucleic acid sequences encoding a protein kinase polypeptide of the invention is provided in which the nucleic acid sequence is expressed only in specific tissue. Methods of achieving tissue-specific gene expression are set forth in International Publication No. WO 93/09236, filed November 3, 1992 and published May 13, 1993.

In all of the preceding vectors set forth above, a further aspect of the invention is that the nucleic acid sequence contained in the vector may include additions, deletions or modifications to some or all of the sequence of the nucleic acid, as defined above.

In another preferred embodiment, a method of gene replacement is set forth. "Gene replacement" as used herein means supplying a nucleic acid sequence which is capable of being expressed *in vivo* in an animal and thereby providing or augmenting the function of an endogenous gene that is missing or defective in the animal.

#### X. Administration of Substances

Methods of determining the dosages of compounds to be administered to a patient and modes of administering compounds to an organism are disclosed in U.S. Application Serial No. 08/702,282, filed August 23, 1996 and International patent publication number WO 96/22976, published August 1 1996, both of which are incorporated herein by reference in their entirety, including any drawings, figures, or tables. Those skilled in the art will appreciate that such descriptions are applicable to the present invention and can be easily adapted to it.

The proper dosage depends on various factors such as the type of disease being treated, the particular composition being used, and the size and physiological condition of the patient. Therapeutically effective doses for the compounds described herein can be estimated initially from cell culture and animal models. For example, a dose can be formulated in animal models to achieve a circulating concentration range that initially

BNSDOCID: <WO\_\_\_\_0073469A2\_I\_>

takes into account the IC<sub>50</sub> as determined in cell culture assays. The animal model data can be used to more accurately determine useful doses in humans.

Plasma half-life and biodistribution of the drug and metabolites in the plasma, tumors, and major organs can be also be determined to facilitate the selection of drugs most appropriate to inhibit a disorder. Such measurements can be carried out. For example, HPLC analysis can be performed on the plasma of animals treated with the drug and the location of radiolabeled compounds can be determined using detection methods such as X-ray, CAT scan, and MRI. Compounds that show potent inhibitory activity in the screening assays, but have poor pharmacokinetic characteristics, can be optimized by altering the chemical structure and retesting. In this regard, compounds displaying good pharmacokinetic characteristics can be used as a model.

Toxicity studies can also be carried out by measuring the blood cell composition. For example, toxicity studies can be carried out in a suitable animal model as follows: 1) the compound is administered to mice (an untreated control mouse should also be used); 2) blood samples are periodically obtained via the tail vein from one mouse in each treatment group; and 3) the samples are analyzed for red and white blood cell counts, blood cell composition, and the percent of lymphocytes versus polymorphonuclear cells. A comparison of results for each dosing regime with the controls indicates if toxicity is present.

20

25

15

5

10

At the termination of each toxicity study, further studies can be carried out by sacrificing the animals (preferably, in accordance with the American Veterinary Medical Association guidelines Report of the American Veterinary Medical Assoc. Panel on Euthanasia, Journal of American Veterinary Medical Assoc., 202:229-249, 1993). Representative animals from each treatment group can then be examined by gross necropsy for immediate evidence of metastasis, unusual illness, or toxicity. Gross abnormalities in tissue are noted, and tissues are examined histologically. Compounds causing a reduction in body weight or blood components are less preferred, as are compounds having an adverse effect on major organs. In general, the greater the adverse effect the less preferred the compound.

For the treatment of cancers the expected daily dose of a hydrophobic pharmaceutical agent is between 1 to 500 mg/day, preferably 1 to 250 mg/day, and most preferably 1 to 50 mg/day. Drugs can be delivered less frequently provided plasma levels of the active moiety are sufficient to maintain therapeutic effectiveness.

5

10

15

Plasma levels should reflect the potency of the drug. Generally, the more potent the compound the lower the plasma levels necessary to achieve efficacy.

### **EXAMPLES**

The examples below are not limiting and are merely representative of various aspects and features of the present invention. The examples below demonstrate the isolation and characterization of the protein kinases of the invention.

EXAMPLE 1: Isolation of cDNA clones Encoding Novel Mammalian Protein Kinases Materials and Methods Identification from cDNA databases and isolation of clones encoding novel protein kinases

Novel kinases were identified from the public EST databases using a Hidden

20

Markov model, abbreviated HMM (Krogh, A., Brown, M., Mian, I. S., Sjolander, K., and Haussler, D. 1994. Hidden Markov models in computational biology: Applications to protein modeling. *J. Mol. Biol.*, 235:1501-1531). The model was built with 70 mammalian and yeast kinase catalytic domain sequences. These sequences were chosen from a comprehensive collection of kinases such that no two sequences had more than 50% sequence identity. ESTs were translated in six open reading frames and were searched against the model. ESTs that had a score of at least 10 against the HMM were then masked for repetitive sequences and vectors and were clustered using MSA. The resulting contigs were searched against known kinases to identify EST clones that encode

25

30

novel kinases.

Approximately 40% of the ESTs encoding potentially novel kinases did not correspond to the correct EST upon sequence analysis. Most of these discrepancies were resolved by ordering additional clones, however, 14 remained unavailable. These 14 ESTs were amplified from a variety of single-stranded cDNA sources with primers derived from the corresponding EST entry as shown on Table 5. The PCR product was subcloned into a bluescript vector, digested to confirm the presence of a correct size insert and sequenced. Full sequencing of EST and PCR was carried out using a cycle sequencing Big-dye kit

with AmpliTaq DNA Polymerase, FS (ABI, Foster City, CA). Sequencing reaction products were run on an ABI Prism 377 DNA Sequencer.

Table 5: Primers used to clone PCR products corresponding to novel kinases

	ID#	ID#	Parent	5' primer	3' primer
sp	na	aa	Sequence	Sequence*	Sequence*
Н	33	153	2R22-5-11	GAGATCGRNTTYAARGA	TGTCACNCCNAGNSWCCAN
				RTTYGA	AYRTT
M	81	200	5R57_10_2_	GCTGCTGGACAGTGACT	GAAAGCAAAGCCTTCACAC
L_			m TESK2_m	TGTATTT	СТТ
Н	67	187	5R69_17_2_h	CTCTCACCTCAGGAACT	GCTTGCGGATCTTCTCA
				GG	
Н	46	166	SGK309_h	GACATCCTGCCGGCCAA	CGGCCCTGGAGCTGCATCA
				CTACG	CTA
M	67	228	5R72_16_2_h	TGCGCGACACCATTGAC	CTCAGGGCTTACATACAGA
				CAG	G
Н	45	165	5R72_8_2_h	AAAGGAGAACTACATTT	CTTCATCATCTCTAATACAT
				TGAAAAT	TGGTTGG
Н	41	161	Z36720	CAAATTAAGATCATTGA	GGAAACAAAGTCCTTGGCC
				CTTTGGG	TC
Н	115	234	AL031652 -	GTGGACATCTGGTCCCT	GTAGGTCCTTCACTCTTGG
			Pak6	CG	AG

degenerate oligonucleotide residue designation:

5 N=A,C,G ot T

R = A or G

Y = C or T

S = C or G

W = A or T

10

15

# Full-length sequence extension of protein kinases using cDNA and genomic databases

Extension of partial cDNA sequences to encompass the full-length open-reading frame was carried out by iterative blastn searching of the cDNA databases listed in Table 6. All blastn searches were conducted using a blosum62 matrix, a penalty for a nucleotide mismatch of -3 and reward for a nucleotide match of 1. The gapped blast algorithm is described in: (Altschul, Stephen F., Thomas L. Madden, Alejandro A. Schaffer, Jinghui Zhang, Zheng Zhang, Webb Miller, and David J. Lipman (1997), "Gapped BLAST and

PSI-BLAST: a new generation of protein database search programs", Nucleic Acids Res. 25:3389-3402).

Table 6. Databases used for cDNA-based sequence extensions

Database	Database Date	
LifeGold templates	Feb 2000	
LifeGold compseqs	Feb 2000	
LifeGold compseqs	Mar 2000	
LifeGold compseqs	Apr 2000	
LifeGold fl	Feb 2000	
LifeGold flft	Apr 2000	
NCBI human Ests	May 2000	
NCBI murine Ests	May 2000	
NCBI nonredundant	May 2000	

5

10

15

20

Extension of partial cDNA sequences to encompass the full-length open-reading frame was also carried out by iterative searches of genomic databases. Three methods were used. The first method made use of the Smith-Waterman algorithm to carry out protein-protein searches of the closest homologue or orthologue to the partial kinase. The target databases consisted of Genescan and open-reading frame (ORF) predictions of all human genomic sequence derived from the human genome project (HGP) as well as from Celera. The complete set of genomic databases searched is shown in Table 7 below. Genomic sequences encoding potential extensions were further assessed by blastp analysis against the NCBI nonredundant to confirm the novelty of the hit. The extending genomic sequences were incorporated into the cDNA sequence after removal of potential introns using the Seqman program from DNAStar. The default parameters used for Smith-Waterman searches were as shown next. Matrix: blosum 62; gap-opening penalty: 12; gap extension penalty: 2. Genescan predictions were made using the Genescan program as detailed in (Chris Burge and Sam Karlin "Prediction of Complete Gene Structures in Human Genomic DNA", JMB (1997) 268(1):78-94). ORF predictions from genomic DNA were made using a standard 6-frame translation.

The second method for genomic sequence-based extensions made use of tBlastn searches of the homologue or orthologue to the partial kinase against the cDNA databases listed in Table 7. The recognition of significant hits in these databases made possible to identify bridging partial cDNA clones. The iterative application of the two methods made possible the assemblage of the virtual full-length sequence for a large number of the kinases presented in this application. All tblastn searches were conducted using a blosum62 matrix, a penalty for a nucleotide mismatch of -3 and reward for a nucleotide match of 1.

The last method for defining cDNA extensions from genomic sequence used iterative searches of genomic databases through the Genescan program to predict exon splicing and the Genewise program (http://www.sanger.ac.uk/Software/Wise2/) to predict potential ORFs based on homology to the closest orthologue/homologue.

Table 7. Databases used for genomic-based sequence extensions

Database	Number of entries	Database Date
Celera v. 1-5	5,306,158	Jan 19/00
Celera v. 6-10	4,209,980	Mar 24/00
Celera v. 11-14	7,222,425	Apr 24/00
Celera v. 15	243,044	May 14/00
HGP all Genescan	25,885	Apr 04/00
HGP; Phase 0	4,944	May 04/00
HGP; Phase 1	28,478	May 05/00
HGP; Phase 2	1,508	May 04/00
HGP; Phase 3	9,971	May 05/00

15

20

5

10

#### Virtual Extensions

Human AA826850 (SEQ ID NO: 3, SEQ ID NO:124)

Blastn analysis of the partial AA826850 sequence revealed an extension to encompass the complete ORF in the Incyte EST 238299.1. A frame-shift correction at position 595 of this EST (marked by X in NA sequence) generated an uninterrupted ORF.

Human AA960957 (SEQ ID NO: 4, SEQ ID NO:125)

10

15

20

25

Since the initial filing of this application, the partial AA960957 sequence appeared in the public database as the full-length gene for a protein kinase encoded by a gene that maps adjacent to the evc (AJ250839) (ellis-van creveld syndrome and weyers acrodental dysostosis) gene from 4p16.1.

Human 5R79-46-1\_h (SEQ ID NO: 5, SEQ ID NO:126)

Blastn analysis of the partial 5R79-46-1 sequence revealed an extension to encompass the complete ORF in the Incyte EST 463894.6. Since the initial filing of this application, the full-length virtual 5R79-46-1 appeared in the public database as the full-length gene for the TANK-binding kinase (TBK1) (Pomerantz, J.L. and Baltimore, D. (1999) EMBO J. 18 (23), 6694-6704). TBK1 participates in NF-kB activation through the formation of a signaling complex with TRAF2 and TANK.

Human AA305176 (SEQ ID NO: 6, SEQ ID NO:127)

Blastn analysis of the partial AA305176 sequence revealed an extension to encompass the complete ORF in the Incyte EST 220937.1.

Human AA256100 (SEQ ID NO: 8, SEQ ID NO:129)

Blastn analysis of the partial AA256100 sequence revealed an extension to encompass the complete ORF through the assembly of three partial clones: Incyte EST 480815.6, KIAA0965 (BAA76809) and AA256100.

Human AA210825 (SEQ ID NO: 9, SEQ ID NO: 130)

Blastn analysis of the partial AA210825 sequence revealed an extension to encompass the nearly complete ORF through the assembly of three partial clones: Incyte EST 014721.7, and the NCBI EST's AW01158 and AA210825. An insertion of two "N's" at positions 1915 and 1916 generated an uninterrupted ORF. Blastx analysis indicated the possibility of a start Met in the range of 400-450 nucleotides (i.e. compared to the closest homolog, human PKCmu (CAA53384.1). However, no Met was found in this region; rather ORF ends in an in-frame stop preceded by the sequence "RGLLAPGDPPCPPPNPAPATPPSSRLPTELFSNFCDS". It is possible that part of the sequence covered by nucleotide positions 1-400 derived from AW01158 comes from an

Human AA127299 (SEQ ID NO:10, SEQ ID NO:131)

intron, explaining the absence of a start Met.

No entries in the database extended this sequence. The 1684 bp insert of this EST contains a 1369 bp intron at the 3' end. Blastx and SW analysis of the 315 bp coding

30

10

15

20

25

30

region revealed homology to the extracatalytic C2 domain of PKC. This EST, may or may not encode a kinase.

Human AA316804 (SEQ ID NO:11, SEQ ID NO:132)

Since the initial filing of this application, the partial AA316804 sequence appeared in the public database as the full-length gene for the PKC family protein kinase EPK2 or PKCnu (AB015982).

Human H19102 (SEQ ID NO:14, SEQ ID NO:135)

Genewise and Genescan analyses of the partial H19102 sequence revealed an extension from the HGP phase 3 contig 3810672 to encompass the complete catalytic domain of this EST. Blastn analysis against the non-redundant database revealed that this gene is found in the cosmid AC005726 from chromosome 17. H19102 may encode a dual catalytic kinase given the homology to S6 kinase. Analysis of genomic sequence upstream of the 5' end of H19102 revealed a non-kinase gene oriented in the same polarity as H19102 suggestive of the start Met for H19102 being close to the 5' end of the H19102 sequence. From this analysis it is deduced that the second catalytic domain of H19102, if present, is most likely located within the 47334-185,215 bp region of the genomic sequence of AC005726.

Human AA476563 (SEQ ID NO:15, SEQ ID NO:136)

Since the initial filing of this application, the partial AA476563 sequence appeared in the public database as the full-length gene for the protein kinase RPS6KC1 (NM\_012424) (Zhang, H. et al Genomics (1999) 61, 314-318), which is an S6 kinase mapping to 12q12-q13.1.

Human AA626690 (SEQ ID NO:16, SEQ ID NO:137)

Since the initial filing of this application, the partial AA626690 sequence appeared in the public database as the full-length gene for the protein kinase RPS6KA6 (AF184965) (Yntema, H.G et al (1999) Genomics 62, 332-343), an S6 kinase commonly deleted in patients with complex X-linked (Xq21.1) mental retardation.

Human AI215680 (SEQ ID NO: 17, SEQ ID NO:138)

Since the initial filing of this application, the partial AI215680 sequence appeared in the public database as the full-length gene encoding a hypothetical protein (AAD30182) from the locus AC006530.4 from chromosome 14.

Human AA887783 (SEQ ID NO:21, SEQ ID NO:142)

10

15

20

25

30

Blastn analysis of the partial AA887783 sequence revealed an extension to encompass the nearly complete ORF through the assembly of three partial clones: Incyte 415390R6 and the NCBI EST's AA887783 and N94726. Since the initial filing of this application, the nearly full-length virtual AA887783 sequence appeared in the public database as the full-length gene encoding SGK3 (AF169035), a serum- and glucocorticoid-induced protein kinase (Kobayashi, T. et al (1999) Biochemical J. 344, 189-197.

Human R47805 (SEQ ID NO:22, SEQ ID NO:143)

A cDNA clone encoding the full-length ORF of R47805 was isolated using R47805 as a screening probe. A full-length form for R47805 has also appeared in the public database as

PTK9L (NM\_007284), an A6-related protein kinase.

Human H60215 (SEQ ID NO:23, SEQ ID NO:144)

Blastn analysis of the partial H60215 sequence revealed an extension to encompass the complete ORF in the public EST AI275726. This was confirmed through the full insert sequencing of this EST (2,310 bp) which corresponds to the sequence under SEQ ID NO:144.

A different stop codon was predicted for AI275726 compared to H60215 due to a single nucleotide insertion at position 1586 in AI275726. Evidence for the extra nucleotide comes from EST AI191922.

SGK324\_h orthologue of W30246\_m (SEQ ID NO:24, SEQ ID NO:145)

Blastn, blastx and Smith-Waterman analyses of genomic databases revealed an extension to encompass the complete ORF corresponding to the human orthologue of murine W30246. Exons predicted from the following sequences were used for contig construction: Celera 17000189645083, 17000057549105 and 11000501939981; Incyte142404.1, HGP\_7249119, Incyte 7196489H1, Celera 11000501939981, 17000028165594; Incyte 7249119\_3, Celera 17000035772368, 11000502081575 and 17000140274329. The latter Celera sequence provides the N-terminus.

Human AA383293 (SEQ ID NO:26, SEQ ID NO:147)

Blastn, blastx and Smith-Waterman analyses of genomic databases revealed an extension to encompass the complete ORF corresponding for AA383293. Exons predicted from the following sequences were used for contig construction: (numbers in parenthesis

10

15

20

25

30

refer to the aa sequence of the closest homolog (RU2S, NP\_057440) used for the Smith-Waterman query): N-term from Incyte 6010175\_2 (14-97), Incyte 6981981 (134-184) 7596749 (186-232) Celera 17000020789545 (243-301) CAB75619.1 (310-341)--(56-145 DCX homology) 6010175\_2, Celera 17000030058129 (241-262 DCX homology).

Human AA021445 (SEQ ID NO:32, SEQ ID NO:152)

Blastn analysis revealed an extension to encompass the nearly complete ORF corresponding for AA021445. Contig reconstruction was as follows: nucleotides1-802 from KIAA0999 (AB023216); nucleotides 803-4321 from full-insert sequence of AA021445. A pairwise alignment between the AA021445 and KIAA0999 revealed three inserts in the extracatalytic C-terminus of 48, 48 and 161 aminoacids. In addition, both AA021445 and KIAA0999 have 15 copies of a CAG repeat. Trinucleotide repeats are often found in genes that linked to neurodegenerative diseases.

Human 2R22-55-1 (SEQ ID NO:33, SEQ ID NO:153)

Blastn analysis revealed an extension in the Incyte EST clone 321074.1 to encompass the complete ORF corresponding to 2R22-55-1.

Human orthologue of AA544838\_m (SEQ ID NO:36, SEQ ID NO:156)

tBlastn analysis identified the partial human KIAA0135 (U79240) clone as the human orthologue of murine AA544838. Blastn revealed an extension KIAA0135\_h (U79240) to encompass the complete ORF. The full ORF was reconstructed from Incyte406786.5, KFZp430051 and KIAA0135 (U79240).

Human orthologue of AI785735\_m (SEQ ID NO:38, SEQ ID NO:158)

tBlastn analysis identified the partial human KIAA0781 (AB018324) clone as the human orthologue of murine AI785735. Blastn revealed an extension KIAA0135\_h (U79240) to encompass the complete ORF. The full ORF was reconstructed from Incyte 986123.37 KIAA0781 (AB018324).

Human AA207220 (SEQ ID NO: 39, SEQ ID NO:159)

Blastn analysis revealed an extension to encompass the nearly complete ORF corresponding for AA021445. The full ORF was reconstructed from Incyte 402740.1 and AA207220. Frame corrections: deletion of 441 and 595 over Inc402740.1 seq based on blastx to keep frame open; two n insertions 940, 941 over AA207220 to keep frame open. Human AA426580 (SEQ ID NO:40, SEQ ID NO:160)

10

15

20

Since the initial filing of this application, the partial AA426580 sequence appeared in the public database as the full-length gene encoding MAK-V (AJ271722) from chromosome 21q22.1.

Human 5R79-54-1 (SEQ ID NO: 41, SEQ ID NO:161)

Genewise and Genescan analyses of the partial 5R79-54-1 sequence revealed an extension from genomic sequence to encode the full ORF for 5R79-54-1.

Human orthologue of AA542015\_m (SEQ ID NO: 42, SEQ ID NO:162)

tBlastn analysis identified KIAA1297 (AB037718). Blastn extended the KIAA1297 sequence to provide the C-terminus through the Incyte 224074.1 EST. The partial ORF consists of a dual catalytic domain flanked by 6 Ig domains and 2 fibronectin repeats. Based on homology to the bt drosophila protein (AAF59316.1), the human form of AA542015 is expected to be missing 16 Ig domains.

Human R19772 (SEQ ID NO:44, SEQ ID NO:164)

The full-length ORF for R19772 was isolated by screening a cDNA library using a probe derived from R19772. Since the initial filing of this application, the R19772 sequence appeared in the public database as the full-length gene encoding Trio (Duet) (AB011422). CDNA library screening revealed multiple isoforms for this gene which are summarized in the Table below.

Table 8. Isoforms for R19772

Kestrl Name	Kestrl	Isoform	Source	Description*
	AA Acc#	type		
Trad (Duet)	R19772	В	Skeletal muscle	Deletion of K at 124
				Deletion of Q at 616
		100		Substitution of E for G at 762
		С	Skeletal muscle	Deletion of K at 124
				Deletion of Q at 616
				Substitution of E for G at 762

		Deletion of 32 aa (160-191)
D	Lung tumor	Deletion of Q at 616
		Deletion of 32 aa (160-191)
E	Lung tumor	Deletion of Q at 616
		Deletion of 32 aa (160-191)

<sup>\*</sup> reference amino acid position are with respect to sequence of Trad (AB011422)

Human AA435956 (SEQ ID NO:48, SEQ ID NO:168)

5

Blastn analysis revealed an extension to encompass the nearly complete catalytic region of AA435956. 5' end sequence extension was provided by genomic locus AC007242.3\_h (range 44880-43801). Based on blastx analysis, the extended sequence encodes is full-length at the C-terminus.

Human AA397553 (SEQ ID NO: 51, SEQ ID NO:171)

10

Since the initial filing of this application, the partial AA397553 sequence appeared in the public database as the full-length gene encoding CRK7 (AF227198), a novel CDC2-related protein kinase that colocalizes with interchromatin granule clusters.

Human AA789239 (SEQ ID NO: 52, SEQ ID NO:172)

15

Since the initial filing of this application, the partial AA789239 sequence appeared in the public database as the full-length gene encoding NKIAMRE (AF130372), a novel kinase deleted in human leukemia.

Human AA631990 (SEQ ID NO:55, SEQ ID NO:175)

20

Blastn analysis revealed an extension to encompass the full-length ORF for AA631990. The full ORF was reconstructed from 253847.5 and AA631990 and AA207220. Frame corrections: delete 1 C at 1380, delete 2N's at 2033/2034.

Human AA557536 (SEQ ID NO:56, SEQ ID NO:176)

Blastn analysis revealed an extension to encompass full-length ORF for AA557536. The full ORF was reconstructed from AA557536, celera 11000504061899 and the Incyte 097089.1 EST. An 85bp intron was removed from AA557536.

25

Human N34132 (SEQ ID NO: 63, SEQ ID NO:183)

Full sequencing of EST N34132 (1.3 kb) confirmed that this cDNA encodes a novel NEK-subfamily kinase. Blast analysis against the EST database showed that four

10

15

20

25

30

EST sequences (AA283140, AA283140, AA282911 and N53011) extended the sequence of N34132 at the 3' end to form a 2.31 kb contig. Blast analysis of the new contig against the nonredunat public database showed that the N34132 extended contig overlapped (100% identity) over 228 bp at its 3' end with human KIAA0344 (AB002342), a 5, 787 bp cDNA encoding a 1246 aa polypeptide. The 5' 790 bp of the KIAA0344 cDNA (encoding the 58 N-terminal protein sequence) were found to be divergent with respect to the extended 2.32 kb N34132 contig. Evidence that the extended N34132 contig (2.31kb) and KIAA0344 (AB002342) belong to the same gene is the following. First, blast analysis of the nucleotide sequences for N34132 and KIAA0344 against the NRN database confirmed that these cDNA's are transcribed from the same genomic locus defined by two overlapping BACs (AC004765 and AC004803) from chromosome 12p13.3. Second, full sequence determination of a PCR fragment amplified from single-stranded cDNA confirmed the junction between the extended N34132 contig and KIAA0344 h (AB002342). The 462 PCR product was amplified with primers CTCCTCAACAGACAGTGCAG (5' primer) and GACATTCTACTACTCGGTCTC (3' primer) designed from the N34132 extended contig and KIAA0344 sequences, respectively. The region of N34132 containing the start Met was isolated by PCR from a testis cDNA library (Clontech).

Human 5R69-17-2 (SEQ ID NO:67, SEQ ID NO:187)

The full-length ORF for 5R69-17-2 was isolated by screening a cDNA library using a probe derived from 5R69-17-2.

Human H85811 (SEQ ID NO:68, SEQ ID NO:188)

Tblastn, Smith-Waterman and blastn analyses using cDNA databases revealed an extension to encompass full-length ORF for H85811. The full ORF was reconstructed from Incyte ESTs 202971.8, 034583.3 and 034583.1 and public ESTs H85811 and AI570599.

Human R43524 (SEQ ID NO:73, SEQ ID NO:192)

Blastn analysis revealed an extension to encompass the complete catalytic region and the C-terminus of R43524. Since the initial filing of this application, the partial R43524 sequence appeared in the public database as the full-length gene encoding the heme-regulated initiation factor 2-alpha kinase (HRI) (AF181071).

Human AA088547 (SEQ ID NO:78, SEQ ID NO:197)

10

15

Genewise and Genescan analyses of genomic databases revealed an extension to encompass the complete ORF for AA088547.

Human orthologue of AA139478\_m (SEQ ID NO:80, SEQ ID NO:199)

Tblastn identified the Incyte 211475.1 as the potential full-length human orthologue of murine AA139478

Human AA232253 (SEQ ID NO:82, SEQ ID NO:201)

The full-length ORF for AA232253 was isolated by screening a cDNA library using a probe derived from AA232253. Since the initial filing of this application, the AA232253 sequence appeared in the public database as the full-length gene encoding SLK (AB011422). SLK is a stress-regulated mixed lineage kinase-like protein that activation of Rac and induction of apoptosis. cDNA library screening revealed multiple isoforms for this gene which are summarized in the Table below.

Table 9. Isoforms for AA232253

Kestrl<br/>NameKestrl AA<br/>Acc #Isoform<br/>typeDescription\*MLK4AA232253MLK4Substitution of C for W at 346MLK4BDifferent Cterm (332-800); seq in MLK4B is as shown in \*

LPLAARMSEESYFESKTEESNSAEMSCQITATSNGEGHGMNPSLQAMMLMGFGDI FSMNKAGAVMHSGMQINMQAKQNSS

20 KTTSKRRGKKVNMALGFSDFDLSEGDDDDDDDGEEEDNDMDNSE

Human H97685 (SEQ ID NO:84, SEQ ID NO:203)

Blastn analysis revealed an extension to encompass the full-length ORF for H97685. The full ORF was reconstructed from Incyte 474824.1 and the public ESTs H97685 and M62021.

Human AI052250 (SEQ ID NO:87, SEQ ID NO:206)

25

<sup>\*</sup> C-terminus specific to MLK4B

Blastn analysis revealed an extension to encompass the full-length ORF for AI052250. The full ORF was reconstructed from Incyte 396868.1, the public partial cDNA FLJ10074 (minus intron) and the public ESTs and the public ESTs AI052250 and H97685, AI499220 and M62021.

5

Human AA278842 (SEQ ID NO:88, SEQ ID NO:206)

A nearly full-length cDNA (FL4F12) for AA278842 was isolated by screening a cDNA library using a probe derived from AA278842. A full-length virtual ORF was generated using FL4F12 and AA278842.

Human AA599286 (SEQ ID NO:89, SEQ ID NO:208)

10

15

20

Since the initial filing of this application, the partial AA599286 sequence appeared in the public database as a full-length ORF (AK000342).

Human AA425725 (SEQ ID NO:90, SEQ ID NO:209)

Since the initial filing of this application, the partial AA425725 sequence appeared in the public database as MSSK1, a serine kinase gene located from human chromosome Xq28.

Human SGK022 orthologue of AA060026\_m (SEQ ID NO:91, SEQ ID NO:210)

Tblastn, Smith-Waterman and blastn analyses of cDNA and genomic databases databases revealed a potential human orthologue for murine AA060026. The full-length ORF for SGK022 was reconstructed from genomic locus AC022307.

Human AA399669 (SEQ ID NO:93, SEQ ID NO:212)

Blastn analysis revealed an extension to encompass the full-length ORF for AA399669. The full ORF was reconstructed as follows: sequence 1-1007 from AL136295.2; sequence 1008-2319 from AA399669 and Incyte 428177.1.

Human AA883975 (SEQ ID NO:95, SEQ ID NO:214)

25

30

Genescan and Genewise analyses of the genomic databases revealed an extension for AA883975 to encompass the full-length ORF

Human AA905446 (SEQ ID NO:96, SEQ ID NO:215)

Tblastn, Smith-Waterman and blastn analyses of cDNA and genomic databases databases revealed an extension for AA905446 to encompass the full-length ORF. For the Smith-Waterman analysis murine STK22 (NP\_033462) was used as the closest orthologue. Contig formation: range 162133-163687 from HGP\_h 6921333\_9; removed intron (146-893) predicted from blastx analysis.

Human H29974 (SEQ ID NO: 97 SEQ ID NO:216)

Blastn analysis revealed an extension to encompass a complete catalytic ORF for AA399669. The nearly full-length ORF was reconstructed using Incyte 213829.1 and H29974.

Human AA215311 (SEQ ID NO:99, SEQ ID NO:218)

Blastn analysis revealed an extension to encompass the full-length ORF for AA21531. The full ORF was reconstructed from Incyte 067584.1, 022456.1, AA215311 and the reverse complement of CPG\_043208.

Human AA018361 (SEQ ID NO:100, SEQ ID NO:219)

10

15

5

The full-length ORF for AA018361 was isolated by screening a cDNA library using a probe derived from AA018361. This yielded clone Sug4-30. Clone Sug4-30, like multiple, independent cDNA clones contained a 181bp intron. The existence of intron-less RNA's was confirmed by a PCR reaction that generated a product that upon sequence analysis skipped the intron region. The full-length virtual ORF for AA018361 was generated through a contig between AL117482 (seq 1-367) and the sequence for clone Sug4-30.

Human orthologue of AA396601\_m (SEQ ID NO:106, SEQ ID NO:225)

20 was

tBlastn and Smith-Waterman analyses of genomic sequence revealed an extension to encompass the full catalytic region for the human orthologue of AA396601. The ORF was reconstructed from Incyte 018653.9 (7261449H1, 6891740J1) and genomic sequence CPG\_040010.

Human orthologue of AA671275 m (SEQ ID NO:108, SEQ ID NO:227)

Since the initial filing of this application, a potential human orthologue for murine AA671275 appeared in the public database as the full-length ORF for vaccinia related kinase 3 (BAA90769).

Human H05721 (SEQ ID NO:111, SEQ ID NO:230)

Genescan and Genewise analyses of genomic sequence revealed an extension to encompass the full-length ORF for H05721.

Human AI086865 (SEQ ID NO:112, SEQ ID NO:231)

30

25

Genescan and Genewise analyses of genomic sequence revealed an extension to encompass the full-length ORF for AI086865. The full-length ORF was reconstructed from Celera 17000102901516, Incyte 243269.1 and public AL1377531.

Human AA836348 (SEQ ID NO:113, SEQ ID NO:232)

Genescan and Genewise analyses of genomic sequence revealed an extension to encompass the full-length ORF for AA836348.

Human R86668 (SEQ ID NO:14, SEQ ID NO:233)

5

The full-length ORF for R86668 was isolated by screening a cDNA library using a probe derived from R86668. Since the initial filing of this application, the R8668 sequence appeared in the public database as the full-length gene mitogen-activated protein kinase kinase 6 (MAP3K6) (NM\_00467).

Human 2R41-9-4 (SEQ ID NO: 16, SEQ ID NO:235)

10

The full-length virtual ORF for 2R41-9-4 was generated using genomic sequence to provide the Nterminus for the partial ORF predicted from clone 2R41-9-4

Table 10. Sequences deleted from the provisional patent due to duplication with other genes in the patent

Prov. SEQ ID NO: (na)	Prov. SEQ ID NO: (aa)
160	196
213	214
215	216
122	126
119	123
148	184
4	20
7	23
205	206
14	30
15	31
35	56
42	63
51	72
44	65
77	91

78	92
79	93
80	94
157	193

### Results

5

10

15

20

25

Table 1 documents the results from the analysis of the nucleic acid sequence data. From left to right the data presented is as follows. "Gene name" refers to the EST or PCR fragment that defined the novel kinase. "Species" refers to the organism the sequence was derived from. "ID#" refers to the nucleic acid and amino acid sequence ID number designation from this patent. "Kinase family "and "Kinase group" refers to the protein kinase classification defined by sequence homology and based on previously established phylogenetic analysis [Hardie, G. and Hanks S. The Protein Kinase Book, Academic Press (1995) and Hunter T. and Plowman, G. Trends in Biochemical Sciences (1977) 22:18-22 and Plowman G.D. et al. (1999) Proc. Natl. Acad. Sci. 96:13603-13610)]. "ORF Start", "ORF End", "ORF Length" refer to the open reading frame range and length as calculated by standard nucleic acid translation programs such as MapDraw (DNAStar). "DNA Repeats" refers to regions of low complexity sequence or repetitive elements such as Alu, LINE, SINE, and LTR sequences. The chromosomal location (CHR localization) for 37 of the 110 novel protein kinases is shown on Table 1 (NA, not available). The methods for determining chromosomal position are outlined below, in Example 2.

Table 2 documents the results from the analysis of the amino acid sequence data. From left to right the data presented is as follows. "Gene name" refers to the EST or PCR fragment that defined the novel kinase. "Species" refers to the organism the sequence was derived from. "ID#" refers to the nucleic acid and amino acid sequence ID number designation from this patent. "Kinase family "and "Kinase group" refers to the protein kinase classification defined by sequence homology and based on previously established phylogenetic analysis [Hardie, G. and Hanks S. The Protein Kinase Book, Academic Press (1995) and Hunter T. and Plowman, G. Trends in Biochemical Sciences (1977) 22:18-22 and Plowman G.D. et al. (1999) Proc. Natl. Acad. Sci. 96:13603-13610)]. "nraa Score", "ID match aa", "Identity", "Similar", "nraa Match Acc#", Description" refer to the data obtained using a Smith-Waterman search of the amino acid sequence against the non-

redundant protein database (Matrix: Pam100; gap open/extension penalties 14/1). "Kinase Domain Start", "Kinase Domain End", "Profile Start" and "Profile End" refer to data obtained using a Hidden-Markov Model to define catalytic range boundaries. The profile has a length of 261 amino acids, corresponding to the complete protein kinase catalytic domain. Proteins in which the profile recognizes a full length catalytic domain have a "Profile Start" of 1 and a "Profile End" of 261. The boundaries of the catalytic domain within the overall protein are noted in the "Kinase Domain Start" and "Kinase Domain End" columns.

### The following abbreviations were used for kinases:

ASK Apoptosis signal-regulating kinase

CaMK Ca2+/calmodulin-dependent protein kinase

CCRK Cell cycle-related kinase

CDK Cyclin-dependent kinase

CK Casein kinase

DAPK Death-associated protein kinase

DM myotonic dystrophy kinase

Dyrk dual-specificity-tyrosine phosphorylating-regulated kinase

GAK Cyclin G-associated kinase

GRK G-protein coupled receptor

GuC Guanylate cyclase

HIPK Homeodomain-interacting protein

IRAK Interleukin-1 receptor-associated kin

MAPK Mitogen activated protein kinase

MAST Micotubule-associated STK

MLCK Myosin-light chain kinase

MLK Mixed lineage kinase

NIMA NimA-related protein kinase

PKA cAMP-dependent protein kinase

RSK Ribosomal protein S6 kinase

RTK Receptor tyrosine kinase

SGK Serum and glucocorticoid-regulated kinase

STK serine threonine kinase

ULK UNC-51-like kinase

# The following abbreviations were used for species

H Human

M Murine

R Rat

FV Fowlpox virus

MT M. thermoautotrophicum

CE Caenorhabditis elegans

DM Drosophila melanogaster

OS Oryza sativa

SP Schizosaccharomyces pombe

TP Tetrahymena pyriformis

PI Petunia inflata

NC Neurospora crassa

MSV Medicago sativa

MSV Moloney murine sarcoma virus

SA Squalus acanthias

CS Cucumis sativus

GM Glycine max

LL Lilium longiflorum

TV Trichomonas vaginalis

MP Mycoplasma pneumoniae

DD Dictyostelium discoideum

SC Saccharomyces cerevisiae

MT Methanobacterium thermoautotrophicum

10

15

20

25

### Domain and Motif Identification

A Hidden Markov model (HMM) (Krogh, A., Brown, M., Mian, I. S., Sjolander, K., and Haussler, D. (1994). Hidden Markov models in computational biology:

Applications to protein modeling. J. Mol. Biol., 235:1501-1531) was used to identify, both catalytic and extracatalytic domains. Table 4 shows extra-catalytic domains that were identified using the HMM program. Other domains such as coiled-coil and pest motifs were identified as described next.

Potential coiled-coil domains were identified using the COILS program (www.ch.embnet.org/software/COILS\_form.html). The matrix used was MTIDK with windows of 14, 21, 28 amino acids. Only regions scoring 0.5 or higher were considered to have potential coiled-coil domain region.

Protein sequences containing potential pest motifs were identified using the program PESTfind (www.at.embnet.org/embnet/tools/bio/PESTfind/). PEST regions in proteins are by definition sequences that tend to be rich in proline, glutamic or aspartic acid, argininine and histidine; they have been associated with increased protein turnover rates (Rogers S. et al. (1986) Science 234, 364-368. The algorithm defines PEST sequences as hydrophilic stretches of amino acids greater than or equal to 12 residues in length. Such regions contain at least one P, one E or D and one S or T. They are flanked by lysine (K), arginine (R) or histidine (H) residues, but positively charged residues are disallowed within the PEST sequence. PESTfind produces a score ranging form about -50 to +50. By definition, a score above zero denotes a possible PEST region; a value greater than +5 defines a high probability that there is a PEST domain.

# Identification of potential coiled-coil domains and PEST domains in N34132

Potential coiled-coil domains were identified in N34132 (SEQ ID NO:183) using the COILS program. Only regions scoring 0.5 or higher were considered to have potential coiled-coil domain region. The amino acid positions within N34231 scoring for potential coil-coil regions are shown below.

Table 11 coiled-coil domains predicted for N34132

Coiled-coil Region	Amino acid range	Length (aa)
1	124-147	24
2	437-451	15
3	495-526	32
4	1,723-1,749	27

Potential PEST domains were identified in N34132 using PESTfind, a value greater than +5 defines a high probability that there is a PEST domain. The amino acid positions within N34132 scoring for potential PEST regions are shown below.

Table 12 Potential Pest domains identified in N34132

PEST Region	Score	Amino acid range	Amino Acid Length
1	+ 4.91	54-95	42
2	+11.4	537-570	34
3	+31.08	1293-1304	12
4	+10.15	1543-1565	23
5	+ 6.17	1698-1732	35

# EXAMPLE 2. Chromosomal Localization of Novel Mammalian Protein Kinases Materials and Methods

Several sources were used to find information about the chromosomal localization of each of the genes described in this patent. First, the accession number for the nucleic acid sequence was used to query the Unigene database. The site containing the Unigene search engine is: http://www.ncbi.nlm.nih.gov/UniGene/Hs.Home.html. Information on map position within the Unigene database is imported from several sources, including the Online Mendelian Inheritance in Man (OMIM,

http://www.ncbi.nlm.nih.gov/Omim/searchomim.html), The Genome Database (http://gdb.infobiogen.fr/gdb/simpleSearch.html), and the Whitehead Institute human physical map (http://carbon.wi.mit.edu:8000/cgi-bin/contig/sts\_info?database=release). For example, searching Unigene with W56561, an EST for a MAK-like kinase, the

20

10

15

5

10

15

20

25

following information is retrieved: Chr.14, D14S65-qTEL. The location of this gene on an "ideogram" of the cytogenetic map of chromosome 14 is also provided, showing that W56561 maps to the bottom of chromosome 14, between 14q31 and 14qTel. If Unigene has not mapped the EST, then the nucleic acid for the gene of interest is used as a query against databases, such as dbsts and htgs (described at http://www.ncbi.nlm.nih.gov/BLAST/blast\_databases.html) containing sequences that have been mapped already. The nucleic acid sequence is searched using BLAST-2 at NCBI (http://www.ncbi.nlm.nih.gov/cgi-bin/BLAST/nph-newblast) and is used to query either dbsts or htgs. In addition to the Whitehead and GDB sites mentioned above, Stanford University maintains a useful site for chromosomal mapping from STS data (http://www-shgc.stanford.edu/RH/rhserverformnew.html). Matches in htgs are often resolved immediately because the genomic region hit is annotated in the htgs entry. If an exact match match is found (defined roughly as 99% identity over a region of about 100 base pairs or longer, excluding any repetitive sequence), then the mapped position of the entry in the database is assigned to the original kinase query. Once a cytogenetic region has been identified by one of these approaches, disease association is established by searching OMIM (see above for URL) with the cytogenetic location. OMIM maintains a searchable catalog of cytogenetic map locations organized by disease. A thorough search of available literature for the cytogenetic region is alo made using Medline (http://www.ncbi.nlm.nih.gov/PubMed/medline.html). References for association of the mapped sites with chromosomal abnormalities found in human cancer can be found in: Knuutila, et al., Am J Pathol, 1998, 152:1107-1123.

#### Results

Table 1. Three of the novel protein kinases were mapped to regions associated with cancer amplicons, as shown on this table. The regions were also cross-checked with the Mendelian Inheritance in Man database, which tracks genetic information for many human diseases, including cancer. References for association of the mapped sites with chromosomal abnormalities found in human cancer can be found in: Knuutila, et al., Am J

Pathol, 1998, 152:1107-1123. Association of these mapped regions with other diseases is

The chromosomal location for 37 of the 110 novel protein kinases is shown on

documented in the Online Mendelian Inheritance in Man (OMIM) (http://www.ncbi.nlm.nih.gov/htbin-post/Omim).

# **EXAMPLE 3: Generation of Specific Immunoreagents**

# 5 Materials and Methods

Peptide sequences to extra-catalytic regions of novel kinases are chosen which are not homologous to other known kinases based on a Smith Waterman homology search against the non-redundant protein database and predicted to be antigenic based on the DNAStar Protean program. These peptides are conjugated to KLH using Glutaraldehyde.

Rabbits are immunized with the KLH-peptide conjugates by four injections three weeks apart. The rabbits are bled ten and fourteen days following the third injection and bled out ten days after the fourth. The serum is checked against the peptide by ELISA.

Table 13. Peptides to be used as immunogens for raising antibodies

Clone	SEQ ID	Peptide Sequence	Amino Location
Name	NO (aa)		
AA8256850	124	KSRDNSRDSSQSEND	339-353
		TEKLKRSQDLPREPLP	372-386
		RGWRPYDIHS	223-232
5R79-46-1	126	FEGPRRNKEVMYK	224-236
		KDDYNETVHKKTE	451-463
		GTHPKDRNVEKLQ	541-553
		EVSKYQEYTNELQET	643-657
AA256100	129	IDDTSNFDDFPESDI	405-419
		TEPDYKSKDWVFL	427-439
		EEKKLRRSQHARKET	61-75
AA210825	130	SNKDTLRKRHYWRLD	507-521
		RHTTRKSSTTLRE	488-500
		FQNNTTNRYYKEIPL	528-542
		GKHRKTGRDVAVK	668-680
		FPTKQESQLRNE	687-698

WO 00/73469

AA316804	132	ESHVHQEPSKRIPS	239-252
		HTKRKSSTMVKEGW	409-422
		PSDLDVERDEEAVK	375-388
		SPGQGKDHKDLSTSI	543-557
R47805	143	EPVGRWDQDYDRAVL	44-58
		KPKGPGGKRGHKRLI	325-339
		PTDVAQLPSRVPRDA	219-233
AA234451	167	DPFDWEKTGNDGSLT	293-307
		HPRPQEKDVWEE	374-385
		RENTDEVFPDEQLSD	340-354
		RSEITQPDRDIPLVR	427-441
AA460132	180	LKSYSTSSKKARPVL	222-236
		KKLDEVRLRGRKRSM	237-251
		ETEKTAQGLSNLAKT	131-145
N34132	183	SGRRRPTKSKGSKS	1848-1862
		PGTAPSKPPLTKAPV	1474-1488
		VDSDTQPKAPGIDD	1365-1378
		AHSLDKTSHSSTTGL	1253-1267
5R69-17-2	187	GTTREKTDRVKST	178-190
		HSEAPELHGKIRSSN	138-152
		DETVTPPQFSIV	87-98
		QYDVKSEIYS	204-213
AA278842	206	TVDPEKSVRDQAFKA	515-529
		DSSTADRWDDEDWGS	637-651
		SVSEDPTQLEEVEKD	539-553
AA836348	232	NAPTKRPRSSTVTEA	323-337
		LDSEEDYYTPQKVDV	514-528
		GDKASYRQPKHVEKL	409-423

# EXAMPLE 4. Expression analysis of Novel Mammalian Protein Kinases GENE EXPRESSION ANALYSIS

Tissue Arrays

5

10

15

20

25

30

"cDNA libraries" derived from a variety of sources were immobilized onto nylon membranes and probed with 32P-labeled cDNA fragments derived from the gene(s) of interest.

Total RNA or mRNA was used as template in a reverse transcription reaction to generate single-stranded cDNAs (ss cDNA) that were tagged with specific sequences at each end. An oligo dT primer containing a specific sequence (CDS:

AAGCAGTGGTAACAACGCAGAGTACT30VN (V=A,G,C N=A,G,C,T)) anneals at the polyA track at the 3' end of the mRNA and the reverse transcriptase (MMLV RnaseH-) transcribes the antisense strand until it reaches the end of the RNA strand when it adds additional C residues. If a primer (SMII:

AAGCAGTGGTAACAACGCAGAGTACGCGGG or ML2G:

AAGTGGCAACAGAGATAACGCGTACGCGGG) ending with 3 Gs is added, it anneals to the added Cs and the MMLV recognizes the rest of the primer sequence as template and continues transcription. As a result, the synthesized cDNAs contain specific sequence tags at both the 5' and the 3' end. When the 5' and the 3' ends are tagged with the same sequence (CDS and SMII) it is referred to as "symmetric." When the 5' end is tagged with a different sequence than the 3' end (CDS and ML2G) is referred to as "asymmetric" A double-stranded "cDNA library" is then generated by PCR amplification using the 3'PCR and ML2 primers (3' PCR: AAGCAGTGGTAACAACGCAGAGT and ML2: AAGTGGCAACAGAGATAACGCGT) that anneal to the added sequence tags.

The amplified "cDNA libraries" were manually arrayed onto nylon membranes with a 384 pin replicator. The DNA was denatured by alkali treatment, neutralized and cross-linked by UV light. The arrays were pre-hybridized with Express Hyb (Clontech) and hybridized with 32P labeled probes generated by random hexamer priming of cDNA fragments corresponding to the genes of interest. After washing, the blots were exposed to phosphorimaging cassettes and the intensity of the signal was quantified. The amount of the DNA on the arrays was also quantified by treating non-denatured or denatured arrays with Syber Green I or Syber Green II respectively (1:100,000 in 50mM Tris, pH8.0) for 2 minutes. After washing with 50mM Tris, pH8.0, the fluorescent emission was detected

with a phosphorimager (Molecular Dynamics) and quantified. The amount of the arrayed DNA was used to normalize the hybridization signal and the corrected values are tabulated in Table 3.

### 5 Results

10

15

20

25

30

The results of the microarray expression analysis of the protein kinases presented in this application is shown in Table 3. Data presentation from left to right is as follows: "Tissue": tissue type of the cDNA; "Tumor sym", indicates that the tissue is derived from a tumor, "sym" refers to the fact that the 5' and 3' primers used to make the sample are the same; "Normal Sym", indicates normal tissue was used to make the sample, with symmetric primers as described above; "Tumor 10", indicates that primary tumor tissue was used to make the cDNA; "Tumor cells", indicates that these cDNA samples were made from cultured tumor cells; "Normal", indicates that these samples are derived from normal tissue or cell lines; "Endos", indicates that these samples are derived from endothelium-related tissue sources; "p53" refers to the status, mutant or wild-type, of the p53 gene in the source samples. Normalized expression values are presented for each gene referred to by its SEQ ID# on the subsequent columns. Genes represented in expression Table 3 are: SEQ ID NO:3 (AA826850), SEQ ID NO:5 (TBK1), SEQ ID NO:6 (AA305176), SEQ ID NO:8 (AA256100), SEQ ID NO:9 (CAB43292), SEO ID NO:11 (EPK2), SEQ ID NO:12 (PKNbeta), SEQ ID NO:14 (H19102), SEQ ID NO:16 (RSK4), SEQ ID NO:17 (AAD30182), SEQ ID NO:20 (SGK2), SEO ID NO:22 (PTK9L), SEO ID NO:26 (AA383293), SEQ ID NO:29 (DRAK2), SEQ ID NO:31 (DRAK1), SEQ ID NO:032 (AA015726), SEQ ID NO:40 (MAK-V), SEQ ID NO:044 (TRAD), SEQ ID NO:044 (TRAD), SEQ ID NO:45 (AA454060), SEQ ID NO:47 (AA234451), SEQ ID NO:48 (AA436054), SEQ ID NO:49 (AA626859), SEQ ID NO:51 (KIAA0904), SEQ ID NO:52 (AA789239), SEQ ID NO:54 (CCRK), SEQ ID NO:55 (CLK4), SEQ ID NO:56 (AA557536), SEQ ID NO:57 (W56561), SEQ ID NO:60 (AA579641), SEQ ID NO:63 (NEK7), SEQ ID NO:66 (CAMKKB), SEQ ID NO:68 (HIPK2), SEO ID NO:72 (R19609), SEQ ID NO:73 (HRI), SEQ ID NO:78 (AA088547), SEQ ID NO:79 (AA449542), SEQ ID NO:082a (MLK4), SEQ ID NO:82 (MLK4b), SEQ ID NO:84 (RIP4), SEQ ID NO:88 (AA278842), SEQ ID NO:89 (AA195964), SEQ ID NO:90 (MSSK1), SEQ ID NO:93 (TSK4), SEQ ID NO:94 (AI025291), SEQ ID NO:95

(AA948538), SEQ ID NO:96 (AA905446), SEQ ID NO:97 (H85389), SEQ ID NO:100 (AA018361), SEQ ID NO:101 (AA311714), SEQ ID NO:110 (AA452647), SEQ ID NO:111 (AA310219), SEQ ID NO:112 (AI086865), SEQ ID NO:114 (MEKK6), and SEQ ID NO:116 (Surtk106).

5

10

15

# EXAMPLE 5. Kinase assays for Erk, JNK1 and p38 MAP kinases

293T cells were transiently transfected with HA- p38 or co-transfected with Flagtagged wt MLK4A, kinase-dead MLK4A, wild-type MLK4B or kinase-dead MLK4B using Lipofectamine 2000 (Lifetech). Cells were lysed 36 hr post-transfection. Cell lysates normalized to contain equivalent amounts of HA-p38 were immunoprecipitated with anti-HA antibody (Mab HA-11, Babco). Immunoprecipitates were split in two portions, one portion was Western-blotted with anti- HA antibody and the other with a phospho-specific p38 antibody (Promega) to detect activated levels of p38. Activation of Erk1 and Jnk1 was measured similarly. (This example applies to AA232253 (SEQ ID NO:82, SEQ ID NO:201).)

# Results:

In transient assays wild-type MLK4A and MLK4B (but not kinase-inactive MLK4A(K45M) or MLK4B(K45M)) activate Erk, JNK1 and p38 MAP kinases. EXAMPLE 6. RAC1 guanine-exchange factor assay

20

25

293T cells were transiently transfected with HA-Rac1 or co-transfected with Flagtagged Duet C, Duet E, Dbl and HA-Tiam-1. Cells were lysed 36 hour post-transfection. Cell lysates normalized to contain equivalent amounts of Rac1 were affinity precipitated with immobilized GST-PBD (p21-binding domain of Pak3). Bound proteins were Western blotted and probed with anti-HA antibody to detect levels of activated Rac1. ((This example applies to R199772 (Trad/Duet)(SEQ ID NO:44, SEQ ID NO:164).)

Results:

Duet C and Duet E both act as guanine nucleotide exchange factors on Rac1.

### **CONCLUSION**

One skilled in the art would readily appreciate that the present invention is well adapted to carry out the objects and obtain the ends and advantages mentioned, as well as those inherent therein. The molecular complexes and the methods, procedures, treatments, molecules, specific compounds described herein are presently representative of preferred embodiments are exemplary and are not intended as limitations on the scope of the invention. Changes therein and other uses will occur to those skilled in the art which are encompassed within the spirit of the invention are defined by the scope of the claims.

10

5

It will be readily apparent to one skilled in the art that varying substitutions and modifications may be made to the invention disclosed herein without departing from the scope and spirit of the invention.

All patents and publications mentioned in the specification are indicative of the levels of those skilled in the art to which the invention pertains.

15

20

The invention illustratively described herein suitably may be practiced in the absence of any element or elements, limitation or limitations which is not specifically disclosed herein. Thus, for example, in each instance herein any of the terms "comprising", "consisting essentially of" and "consisting of" may be replaced with either of the other two terms. The terms and expressions which have been employed are used as terms of description and not of limitation, and there is no intention that in the use of such terms and expressions of excluding any equivalents of the features shown and described or portions thereof, but it is recognized that various modifications are possible within the scope of the invention claimed.

25

In particular, although some formulations described herein have been identified by the excipients added to the formulations, the invention is meant to also cover the final formulation formed by the combination of these excipients. Specifically, the invention includes formulations in which one to all of the added excipients undergo a reaction during formulation and are no longer present in the final formulation, or are present in modified forms.

30

In addition, where features or aspects of the invention are described in terms of Markush groups, those skilled in the art will recognize that the invention is also thereby described in terms of any individual member or subgroup of members of the Markush

group. For example, if X is described as selected from the group consisting of bromine, chlorine, and iodine, claims for X being bromine and claims for X being bromine and chlorine are fully described.

Other embodiments are within the following claims.

WO 00/73469 PCT/US00/14842

133

What is claimed is:

## **CLAIMS**

An isolated, enriched, or purified nucleic acid molecule encoding a kinase 1. polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ 5 ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEO ID NO:133, SEO ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ 10 ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168. SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEO ID NO:173, SEO ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ 15 ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEO ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ 20 ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEO ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEO ID NO:213, SEO ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ 25 ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

- 2. The nucleic acid molecule of claim 1, wherein said nucleic acid molecule comprises a nucleotide sequence that:
- encodes a polypeptide comprising the amino acid sequence set forth (a) in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID 5 NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID 10 NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEO ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEO ID NO:175, SEO ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID 15 NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID 20 NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEO ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEO ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID 25 NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242;
  - (b) is the complement of the nucleotide sequence of (a);
- 30 (c) hybridizes under highly stringent conditions to the nucleotide molecule of (a) and encodes a naturally occurring kinase polypeptide;

PCT/US00/14842

- (d) encodes a kinase polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEO ID NO:128, SEO ID NO:129. SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, 5 SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEO ID NO:139. SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149. SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEO ID NO:153, SEO ID NO:154. SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, 10 SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEO ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, 15 SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, 20 SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, 25 SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, except that it lacks one or more, but not all, of a domain selected from the group consisting of an N-terminal domain, a catalytic domain, a C-terminal domain, a coiled-coil structure region, a proline-rich region, a spacer region, an insert, and a C-terminal tail;
- 30 (e) is the complement of the nucleotide sequence of (d);

- encodes a domain of an amino acid sequence selected from the (f) group set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEO ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, 5 SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEO ID NO:145. SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. 10 SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEO ID NO:205. SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEO ID NO:215. SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, wherein said domain is selected from the group consisting of an N-terminal domain, a catalytic domain, a C-terminal domain, a coiled-coil structure region, a proline-rich region, a spacer region, an insert, and a C-terminal tail;
  - (g) is the complement of the nucleotide sequence of (f):
- 30 (h) encodes a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEO ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID

20

25

WO 00/73469 PCT/US00/14842

137

NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID 5 NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID 10 NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID 15 NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEO ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEO ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID 20 NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, except that it lacks one or more, but not all, of the domains selected from the group consisting of an N-terminal domain, a catalytic domain, a C-terminal domain, a spacer region, a proline-rich region, a coiled-coil structure 25 region, and a C-terminal tail; or

- (i) is the complement of the nucleotide sequence of (h).
- 3. The nucleic acid molecule of claim 1, further comprising a vector or promoter effective to initiate transcription in a host cell.

30

- 4. The nucleic acid molecule of claim 1, wherein said nucleic acid molecule is isolated, enriched, or purified from a mammal.
  - 5. The nucleic acid molecule of claim 4, wherein said mammal is a human.
- 6. A nucleic acid probe for the detection of nucleic acid encoding a kinase polypeptide in a sample, wherein said polypeptide is selected from the group consisting of 5 SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEO ID NO:126. SEO ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136. SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEO ID NO:146. 10 SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, 15 SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, 20 SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, 25 SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, 30 and SEQ ID NO:242.

BNSDCCID: <WO\_\_\_\_\_0073469A2\_I\_>

7. The probe of claim 6, wherein said polypeptide is a fragment of the protein encoded by an amino acid sequence selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID 5 NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEO ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID 10 NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID 15 NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEO ID 20 NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEO ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID 25 NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

8. A recombinant cell comprising a nucleic acid molecule encoding a kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ 5 ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ 10 ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ 15 ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ  ${\rm I\!D}$  NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ 20 ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ 25 ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

	9. The cell of claim 8, wherein said polypeptide is a fragment of a protein
	encoded by an amino acid sequence selected from the group consisting of SEQ ID
	NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID
	NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID
5	NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID
	NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID
	NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID
	NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID
	NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID
10	NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID
	NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID
	NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID
	NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID
	NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID
15	NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID
	NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID
	NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID
	NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID
	NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID
20	NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID
	NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID
	NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID
	NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID
0	NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID
25	NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID
	NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEG
	ID NO:242.

10. An isolated, enriched, or purified kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEO ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEO ID NO:135. 5 SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140. SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145. SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155. SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, 10 SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEO ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175. SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, 15 SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190. SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, 20 SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215. SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, 25 SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.

- 11. The polypeptide of claim 10, wherein said polypeptide is a fragment of the protein encoded by an amino acid sequence selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEO ID NO:133, SEO ID NO:134, SEO ID NO:135, SEO ID NO:136, SEO ID 5 NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID 10 NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID 15 NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEO ID NO:208, SEO ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID 20 NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID 25 NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.
  - 12. The polypeptide of claim 10, wherein said polypeptide comprises:
- (a) an amino acid sequence selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ

10

15

20

25

30

ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEO ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ. ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242;

(b) an amino acid sequence selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ

10

15

20

25

30

ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEO ID NO:196, SEO ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEO ID NO:216, SEO ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEO ID NO:226, SEO ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEO ID NO:236, SEO ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, except that it lacks one or more, but not all of the domains selected from the group consisting of an N-terminal domain, a catalytic domain, a C-terminal domain, a spacer region, a proline-rich region, a coiled-coil structure region, and a C-terminal tail

(c) a domain of an amino acid sequence selected from the group set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:177, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ I

NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242 wherein said domain is selected from the group consisting of a C-terminal domain, a catalytic domain, an N-terminal domain, a spacer region, a proline-rich region, a coiled-coil structure region, and a C-terminal tail.

15

20

25

30

10

- 13. The kinase polypeptide of claim 10, wherein said polypeptide is isolated, purified, or enriched from a mammal.
  - 14. The kinase polypeptide of claim 13, wherein said mammal is a human.
- 15. The kinase polypeptide of claim 10, wherein said polypeptide is a AA144574, AA116841, AA256100, AA305176, AA210825, AA316804, AA980090, N42050, AA476563, AA626690, AA960957, H19102, AA045601, AA107515, AA109508 or AA887783 polypeptide.
- 16. The kinase polypeptide of claim 10, wherein said polypeptide is a H60215, AA197883, AA297313, W30246, AA172300, AA383293, AA542015, H01248, N23936, W44160, 2R22-5-11, 5R72-18-1, AA021445, AA207220, AA426580, AA544838, W90839, 5R79-54-1, AA839940, R19772 or 5R72-8-2 polypeptide.
- 17. The kinase polypeptide of claim 10, wherein said polypeptide is a AA234451 polypeptide.
- 18. The kinase polypeptide of claim 10, wherein said polypeptide is a 5R65-16-1, AA061797, AA065538, AA124976, AA397553, AA435956, AA575635, AA626859, AA789239, AI086865, H17727, H29974, AA557536 or N28606 polypeptide.
- 19. The kinase polypeptide of claim 10, wherein said polypeptide is a AA631990 or W08549 polypeptide.

- 20. The kinase polypeptide of claim 10, wherein said polypeptide is a 5R72-16-2, R19927 or R43524 polypeptide.
- 21. The kinase polypeptide of claim 10, wherein said polypeptide is a 5R57-10-2 polypeptide.
- 5 22. The kinase polypeptide of claim 10, wherein said polypeptide is a AA232253 polypeptide.
  - 23. The kinase polypeptide of claim 10, wherein said polypeptide is a AA430250, AA836348, R86668 or N34132 polypeptide.
  - 24. The kinase polypeptide of claim 10, wherein said polypeptide is a AA098024or SuRTK106 polypeptide.
  - 25. The kinase polypeptide of claim 10, wherein said polypeptide is a R47805, AA099102, AA589241, H85811, AA013524, AA452647, AA840598, AA088547, AA139478, AA826850, R87679, W65887, H97685, W20810, AA599286, AA425725, AA103218, AA711829, AA060026, AA399669, AA758539, AA883975, AA948538, AA018361, AA215311, AA311714, AA498104, 5R69-17-2, 5R69-23-3, 5R69-26-2, AA118352, AA396601, AA671275, AA278842, AA460132 or H05721 polypeptide.

- An antibody or antibody fragment having specific binding affinity to a 26. kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID 5 NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID 10 NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID 15 NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID 20 NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID 25 NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.
  - 27. The antibody or antibody fragment of claim 26, wherein said polypeptide comprises:
- (a) an amino acid sequence selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ

WO 00/73469 PCT/US00/14842

149

ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEO ID NO:140, SEO ID NO:141, SEO ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEO ID NO:156, SEO ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEO ID NO:161, SEO ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEO ID NO:176, SEO ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEO ID NO:231, SEO ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242;

(b) an amino acid sequence selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ

5

10

15

20

25

10

15

20

25

30

ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEO ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEO ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, except that it lacks one or more, but not all, of the domains selected from the group consisting of a C-terminal domain, a catalytic domain, an N-terminal domain, a spacer region, a proline-rich region, a coiled-coil structure region, and a C-terminal tail.

(c) a domain of an amino acid sequence selected from the group set forth in SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:134, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:178, SEQ ID NO:184, SEQ ID NO:185, SEQ I

10

NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:231, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:234, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242 wherein said domain is selected from the group consisting of a C-terminal domain, a catalytic domain, an N-terminal domain, a spacer region, a proline-rich region, a coiled-coil structure region, and a C-terminal tail.

- 28. A hybridoma which produces an antibody having specific binding affinity to a kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID 5 NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEO ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID 10 NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID 15 NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEO ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEO ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID 20 NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEO ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEO ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEO ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID 25 NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.
  - 29. A method for identifying a substance that modulates kinase activity comprising:
- (a) contacting a kinase polypeptide selected from the group consisting

  SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126,

  SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131,

  SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136,

SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEO ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEO ID NO:157, SEO ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, 5 SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEO ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEO ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, 10 SEO ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEO ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEO ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, 15 SEO ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEO ID NO:222, SEO ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, 20 SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242 with a test substance;

- (b) measuring the activity of said polypeptide; and
- (c) determining whether said substance modulates the activity of said polypeptide.
  - 30. A method for identifying a substance that modulates kinase activity in a cell comprising:
- (a) expressing a kinase polypeptide in a cell, wherein said polypeptide is selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID

NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEO ID NO:148, SEO ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID 5 NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID 10 NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID 15 NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID 20 NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242;

- (b) adding a test substance to said cell; and
- (c) monitoring a change in cell phenotype or the interaction between said polypeptide and a natural binding partner.

- A method for treating a disease or disorder by administering to a patient in 31. need of such treatment a substance that modulates the activity of a kinase selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEO ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID 5 NO:135, SEO ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEO ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEO ID NO:156, SEO ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID 10 NO:160, SEO ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID 15 NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID 20 NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEO ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID 25 NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242.
  - 32. The method of claim 31, wherein said disease or disorder is selected from the group consisting of immune-related diseases and disorders, cardiovascular disease, neurodegenerative disorders, and cancer.
  - 33. The method of claim 31, wherein said substance modulates kinase activity in vitro.

- 34. The method of claim 33, wherein said substance is a kinase inhibitor.
- 35. A method for detection of a kinase polypeptide in a sample as a diagnostic tool for a disease or disorder, wherein said method comprises:
- (a) contacting said sample with a nucleic acid probe which hybridizes 5 under hybridization assay conditions to a nucleic acid target region of a kinase polypeptide selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEO ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEO ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, 10 SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEO ID NO:160, SEO ID NO:161, SEO ID NO:162, SEO ID NO:163, SEO ID NO:164. SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, 15 SEQ ID NO:170, SEQ ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, 20 SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, 25 SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, 30 SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, said probe comprising the nucleic acid sequence encoding said polypeptide, fragments thereof, or the complements of said sequences and fragments; and

- (b) detecting the presence or amount of the probe:target region hybrid as an indication of said disease.
- 36. The method of claim 35, wherein said disease or disorder is selected from the group consisting of immune-related diseases and disorders, cardiovascular disease, neurodegenerative disorders, and cancer.
- 37. A method for detection of a kinase polypeptide in a sample as a diagnostic tool for a disease or disorder, wherein said method comprises:
- (a) comparing a nucleic acid target region encoding said kinase polypeptide in a sample, wherein said kinase polypeptide is selected from the group consisting of SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ 10 ID NO:126, SEQ ID NO:127, SEQ ID NO:128, SEQ ID NO:129, SEQ ID NO:130, SEQ ID NO:131, SEQ ID NO:132, SEQ ID NO:133, SEQ ID NO:134, SEQ ID NO:135, SEQ ID NO:136, SEQ ID NO:137, SEQ ID NO:138, SEQ ID NO:139, SEQ ID NO:140, SEQ ID NO:141, SEQ ID NO:142, SEQ ID NO:143, SEQ ID NO:144, SEQ ID NO:145, SEQ 15 ID NO:146, SEQ ID NO:147, SEQ ID NO:148, SEQ ID NO:149, SEQ ID NO:150, SEQ ID NO:151, SEQ ID NO:152, SEQ ID NO:153, SEQ ID NO:154, SEQ ID NO:155, SEQ ID NO:156, SEQ ID NO:157, SEQ ID NO:158, SEQ ID NO:159, SEQ ID NO:160, SEQ ID NO:161, SEQ ID NO:162, SEQ ID NO:163, SEQ ID NO:164, SEQ ID NO:165. SEQ ID NO:166, SEQ ID NO:167, SEQ ID NO:168, SEQ ID NO:169, SEQ ID NO:170, SEQ 20 ID NO:171, SEQ ID NO:172, SEQ ID NO:173, SEQ ID NO:174, SEQ ID NO:175, SEQ ID NO:176, SEQ ID NO:177, SEQ ID NO:178, SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:183, SEQ ID NO:184, SEQ ID NO:185, SEQ ID NO:186, SEQ ID NO:187, SEQ ID NO:188, SEQ ID NO:189, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:199, SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ 25 ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, SEQ ID NO:216, SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ 30 ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO:224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ

ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, SEQ ID NO:240, SEQ ID NO:241, and SEQ ID NO:242, or one or more fragments thereof, with a control nucleic acid target region encoding said kinase polypeptide, or one or more fragments thereof; and

- (b) detecting differences in sequence or amount between said target region and said control target region, as an indication of said disease or disorder.
- 38. The method of claim 37, wherein said disease or disorder is selected from the group consisting of immune-related diseases and disorders, cardiovascular disease, neurodegenerative disorders, and cancer.

BNSDOCID: <WO\_\_\_\_\_0073469A2\_!\_>

			_	_	. ,		_	<u> </u>	_		_	,	,	,_	_	,	_		_		_	_	_			_						_	_		_	.,		_	,	_	_	_		_	_	_			_	,	,		٠,	_	<u>.</u>	<del>-,-</del>	<del>, ,</del>
CHR locafization	22q11	¥.	NA	4010.1	NA.	211001	12011	10013-013 3		2021	¥N	W	CHR17	12q12-q13.1	Xa21.1	14924.3	6q21-q22	NA.	NA	NA	3014.3	1p31.1-1p32.3	NA	NA	¥	Ą	2q31-2q24.3	NA	91-110 7211-911	11922.1-11922.3	YA YA	Y Y	2q34-q37	NA	NA	Α¥	21911	¥.	NA.	3013 3-021	11015.1-11015.2	NA	NA	NA NA	¥N.	Y.	FA22 422 1	0.02p-02pc	NA NA	A N	NA.	14932	NA	¥N.	20q12 Amplicon	NA NA	12p13.33
DNA Repeats	×		285-304	×	*	× ,	,	,		×	2221-2280	Γ	599-638	*	*	767-786	656-683	1804-1830	×	×	×		208-227		439-458	×	×	×	91-110	A4 2201 4250 42	71-0071, 1530-15	×	×	1002-1022	*	×	×	×	× ×		*	843-862	×	×	84-110	X	1218-1238		161,101	*	516-536	×	×	×	* ,	« »	×
ORF_Length	2064	1134	1257	1242	2187	204	1303	2014	315	2870	2067	615	1152	1407	2235	1847	1293	1290	732	1338	1047	1320	2076	891	2058	2418	1	1	1	ı		1580	3990	069	2778	1887	2142	2622	381	3861	1542	1524	1434	798	741	000	1802	700	633	1497	1635	1257	1896	1239	138	843	5856
ORF end	5064	1135	1264	1306	2278	850	2477	3050	315	2670	2687	616	1152	1407	2235	1647	1293	1364	733	1373	1047	1738	2082	891	2058	2418	1380	1286	2521	9178	2187	1560	4088	692	2832	1989	2142	7797	381	3861	1947	1620	1839	208	742	4470	1807	100	63	1530	1684	1257	1896	1239	1386	944	2897
ORF Start	- -	2	80	65	8 3	3	88	213	-	-	-	2	-	-	-	-	1	75	2	36	-	420	7	-	-	-	262	121	-	140	-	-	11	3	155	103	-	- -	-	-	408	16	406	-	7	7	- 4	)  -		56	8	-	-	- 6	<u> </u>		42
Length AA	8	378	418	=	729	375	8 8	650	502	980	688	502	384	469	745	248	431	430	244	446	349	440	692	297	989	808	373	372	-	838	222	520	1330	230	926	628	7.1	2286	127	1287	514	508	478	568	747	V071	71.5	137	211	667	545	419	632	113	3 8	381	1952
Length NA																																1594					2145													2488	1831	1260	1899	17.8	200	2326	1328
Group	Š	GRK	Ma3C11.1 ce	Mo3C11.1 ce	Mo3C11.1 ce	200	5 5	C C	PKG	PKC	PKC	PKC	S6K	Sek	Sex	X9S	SGK	SGK	SGK	SGK	A6	AMPK	CAMIK	CAMK	CAMK	CAMK	DAPK	DAPK	DAPK	FARK	FAR	EME	EMK	EMK	EMĶ	Ž.	EMK	MLCK	L OIL	Tro	Unique	કૅ	Š	SOK	ž	Š	Š	į	Š	CLK	Š	Ş	Š	ğ	75K72 SC	C28C2 G8	C26C2 ce
Family	AGC	1	7	T	Т	Т	Т	Т	Т	Π		Γ				П				П				CAMK	П	CAMK		Т	CAME	Т	Т	S S		CAMK	Т	CAMK	CAMK	Z Z	CAMK	Π		ક	ક	CWGC	CMC	2000	CMGC	2000	CMGC	CMGC	CMGC	SMSC	CMGC	SMO	Microbial PK	100	Other
SEO ID # 33	122	123	124	125	126	177	971	027	131	132	133	134	135	136	137	138	139	140	141	142	143	144	145	146	147	148	148	150	2	261	3	55	156	157	158	653	<u>چاچ</u>	101	163	191	165	168	167	168	109	1/1	177	52	2 2	175	176	111	178	6/1	3 2	182	183
SEQ ID # na	-	2	6	•	S	9	,		10	Ξ	12	13	7	15	92	17	18	19	20	21	22	23	24	52	28	88	28	8	15	35	3	8	38	37	8	39	60	-	43	=	45	46	47	46	9	3	52	5 6	3 3	SS	95	57	58	65	3 2	95	83
rov Seq ID_AA	×	17	178	22	208	18,20	07'01	-	707	22	24	×	28	22	26	228	×	×	29	32	167	54	×	57	59	\$3	58	×	93	8 2	5	20	×	88	×	67	88	,	6	73	74	185	78	98	8 ,	. 8	8			101	103	104	*	*	201	183	126
Prov. Seq. 10, NA Pr	×	-	140	=	207	25	,,,	•	203	ø	80	*	12	da	2	227	×	×	13	16	131	33	×	98	88	34	37	* !	9 4	9	2,	<b>6</b>	*	48	×	9	43	30	30	52	53	159	75	85	<b>3</b>	4 6	2 2	3 .		8	69	8	-	***		147	122
SP Pro	¥	Σ	I	I	I	Į	Σ 3	c 3		I	Ī	Σ	I	I	I	I	I	Σ	×	=	Ξ	Ŧ	H	Σ	I	Σ	Ŧ	Σ:	<u> </u>	c   3	= =	.  ≥	Ξ	Σ	Ŧ	I.	Ξ:	=	12	I	Ŧ	I	∓   	Ξį:	El 2	: E I	=	2	: E  2	İ	I	I	Ι.	<b>2</b> ::	Į.	E . 3	Ŧ
П	X69117 h BARK2 h	1	٦	Π	T		T	2 4	AA127299 h	A h. EPK2	N42050 h PKNbeta	Al021023 m PKNbela m	۽	33 h RPS6KC1	30 h RSK4	30 h		15 m	J8 m	AABB7783 h SGK3, SGKL	h PTK9L	£	SGK324_h	m SGK324 m	93 h	83 m	AA172300 h DRAK2	W44150 m DRAK2 m	H01248 h, DRAK1 h	4	1 h AAC33487	W90839 m	5 h	AA544838 m 406786 m	35 h	20 h	AA426580 h, MAK V h	6	15 m SGKOBB m	-	2 h	=	51 h	95 h	06 h	53 h CDK7	AA780210 h	76 m	44575635 m CCRK m	90 h CLK4	36 h	N28606 h, MOK	53 h, ICK	#0 m	32 h	18 m SCK034 m	NEK7 h, N34132 h
	X69117	AA14457	AAB26B5	AA96095	5R79-46	AA305176 h	AA1100	10070	AA1272	AA31680	N42050	A102102	H19102 h	AA47656	AA6268	AA21568	SGK 1	AA1075	AA 1095(	AABB77	R47805	H60215 h	SGK324	W30246	AA383293 h	AA1978	A1723	W44160	H01248	2022	03137	W90839	406786.5 h	AA544B.	AA7857.	AA2072.	AA4285	07/067	AA5420	R19772	5R72 B	SGK309	AA2344.	AA4359	AA626B	44 307 6	A 7802	1240	A A 5756	AA6319	AA557536 h	N28606	AB0231	AA8399	AA4601	A 1032	NEK7

_
0
₹
ខ
_
_
Φ
ᅙ
ਰ
⊢

a
ö
ă
Ø

Maintain   Maintain	60	Ī	T	1	T	1	1	Ī					Τ	-			7				-	_	i	i		i	ī	7	1	i	_	ì	-	1	Ţ	Ţ	Т	1	1		ļ	i	İ	į	1	<del>-</del>		:	;	:	•	٦
Ramily         Cross         Length         Inch         Inch         Total         Total         Michael	Profil	pua		781	<b>5</b> 8	791	281	261	261	261	261	281	261	261	261	261	261	261	261	261	261	561	261	261	261	261	797	261	261	261	261	261	281	261	261	13		200	28.1	28.	ğ	2 8	9 3	261	261	791	261	261	261	261	261	261
France   Court   Co	Profile	start	arair.	-	121	-	-	-	-	242	-	-	256	-	-	126	-	-	-	-	-	-	24	-	253	-	-	-	-	-	-	-	-	-	-		- ,	- -	- 22	3 -	- -	- -	-  -	-	-	186	-	-	-	-	23	23
Page   Page	Domain (s)	pue	210	453	143	286	283	304	310	44	383	907	24	832	818	134	333	459	330 & 683	539	355	354	169	369	17	333	625	297	673	771	293	293	321	259	325		307	240	1530	27.4	100	500	920	825	873 & 1356	78	1239	381	313	471	218	191
Page   Page	Domain(s)	Fiart	11816	<u>=</u>	6	92	23	6	35	54	06	651	2	576	559	1	81	225	73 & 426	153	98	98	1	162	10	6	368	59	415	514	33	32	61	80	74		g (	B	£ 4	-   5	3 5	3 3	5 E	270	320 & 1086	8	985	116	34	21	-	7
Family         Group         Proces         as         as         length         Mile           AGC         GRK         2.7e-314         686         667         100         100           AGC         GRK         1.30E-180         378         371         96         89           AGC         GRK         1.30E-180         378         371         96         89           AGC         0.3C111 cels 1.30E-180         38         729         729         100         100           AGC         0.3C111 cels 1.30E-180         38         73         46         86         89           AGC         0.3C111 cels 1.30E-181         48         483         100         100         100           AGC         O.SCI 1.10E-10         1729         7.29         100         100         100           AGC         NDR         6.0E-181         88         10         100         100           AGC         PKC         1.10E-10         105         42         42         10         100           AGC         PKC         1.10E-10         105         100         100         100           AGC         PKC         1.0E-18         89	0		Describuon	BARK2 [Homo sapiens]	Adrenergic receptor kinase, beta 2 (G-protein-linked receptor kin	Serine/threonine protein kinase [Homo saplens]	Serine/threonine protein kinase [Homo sapiens]	TANK-binding kinase 1 [Homo sapiens]	KIAA0973 protein [Homo sapiens]	CG7719 gene product [Drosophila melanogaster]	KIAA0965 protein [Homo saplens]	Protein kinase C. mu (Homo sapiens)	Protein kinase C. BETA-II TYPE (PKC-BETA-2) [Homo sapiens]	Protein kinase C, nu (Homo saptens)	PKNbeta [Homo sapiens]	Protein kinase N beta [Homo sapiens]	Ribosomal protein S6 kinase 3 [Homo sapiens]	Ribosomal protein S6 kinase, 52kD, polypeptide 1 [Homo sapien	Ribosomal protein S6 kinase, 90kD, polypeptide 6 [Homo sapien	Unknown [Homo sapiens]	SGK [Homo saplens]	Serum/glucocorticoid regulated kinase [Mus musculus]	Protein kinase [Homo saplens]	SGK-like protein SGKL [Homo saplens]	Protein tyrosine kinase 9-like (A6-related protein) [Homo sapiens	Phosphoprotein [Homo saplens]	DCAMKL1 (DOUBLECORTIN-LIKE AND CAM KINASE-LIKE 1)	CPG16 [Mus musculus]	DCAMKL1 (DOUBLECORTIN-LIKE AND CAM KINASE-LIKE 1)	CPG16 (Mus musculus)	Death-associated protein kinase-related 2	Death-associated protein kinase-related 2	Death-associated protein kinase-related 1	KIAA0999 protein [Homo saplens]	Hypothetical protein F49C5.4 - [Caenorhabditis elegans]	Cdc25C associated protein kinase C-TAK1 [Homo sapiens]	Cdc25C associated protein kinase C-TAK1 [Homo sapiens]	K3123/ 1, partial CUS (Homo sapiens)	MAAO 133 gene is related to pint-1 ortogene, monito saprens	VIAAA784 profess (Homo epologe)	Caracter From Control adplication	Nivados/ gene product (noting sapiens)	Hormonally upregulated neu tumor-associated kinase inomo sa			KIAA1297 protein [Homo sapiens]	STK with Dbl- and pleckstrin homology domains [Homo sapiens	MLCK (Dictyostelium discoideum)	CG11533 gene product [Drosophila melanogaster]	CG11533 gene product [Drosuphila melanogaster]	PFTAIRE protein kinase 1 [Homo sapiens]	Cyclin-dependent kinase-like 1 (CDC2-related kinase) [Homo sa
Family         Group         Pacore         aa         length         W           AGC         GRK         2.76-314         688         687         100           AGC         GRK         1.30E-190         378         371         98           AGC         GRK         1.30E-190         378         371         98           AGC         OSC11.1 ce         1.20E-09         329         73         46           AGC         OSC11.1 ce         1.30E-19         88         42         49           AGC         OSC11.1 ce         1.30E-19         329         73         46           AGC         OSC11.1 ce         1.30E-19         329         73         46           AGC         ONDR         1.20E-09         329         73         46           AGC         ONDR         1.00E-18         42         49           AGC         PKC         1.10E-10         105         42         42           AGC         PKC         1.10E-10         105         42         42           AGC         PKC         1.10E-10         105         42         42           AGC         PKC         1.00E-13         43	Match	#UV	ACC#	CAB45657.1	NP 037029.1	CAB76471.1	CAB76471.1	INP 037386.1	BAA76817.1	AAF 55594.1	BAA76809.1	NP 002733.1	P05127	NP 005804.1	NP 037487.1	JC7083	AAC82495.1	NP 036556.1	NP 055311.1	AAD30182.1	AAD41091.1	NP 035491.1	AAF12757.2	AAF27051.1	NP_009215.1	CAA04119.1	015075	AAF26675.1	015075	AAF26675.1	NP 004217.1	NP 004217.1	NP 004751.1	BAA76843.1	T22427	AAC15093.1	AAC15093.1	AAC33487.1	DAA09404.1	DA A 24504 4	10040040	NP (00000).	NF U00401.1	AAA73168.1	BAA92535.1	BAA92535.1	NP_008995.1	P25323	AAF 59340.1	AAF59340.1	NP 036527.1	NP 004187.1
Family         Group         Pecore         aa         lb           AGC         GRK         2.76-314         688         687         100           AGC         GRK         1.30E-180         378         371         98           AGC         GRK         1.30E-180         378         371         98           AGC         0.3011.1 cet 1.30E-180         378         371         98           AGC         0.3011.1 cet 1.30E-180         378         73         46           AGC         0.3011.1 cet 1.30E-180         329         7.3         46           AGC         NDR         1.20E-09         329         7.3         46           AGC         NDR         1.20E-181         444         493         40           AGC         NDR         1.20E-181         484         483         40           AGC         PKC         1.10E-10         105         42         49           AGC         PKC         1.10E-10         105         42         49           AGC         PKC         1.10E-10         105         42         40           AGC         PKC         1.20E-13         434         40         100 <td>*</td> <td>Cimilar</td> <td>SIMILIZ</td> <td>90</td> <td>66</td> <td>98</td> <td>100</td> <td>100</td> <td>99</td> <td>1</td> <td>5</td> <td>8</td> <td>57</td> <td>5</td> <td>100</td> <td>92</td> <td>55</td> <td>100</td> <td>5</td> <td>100</td> <td>5</td> <td>66</td> <td>5</td> <td>88</td> <td>9</td> <td>91</td> <td>11</td> <td>83</td> <td>9</td> <td>73</td> <td>100</td> <td>95</td> <td>100</td> <td>8</td> <td>2</td> <td>65</td> <td>9</td> <td>3</td> <td>30</td> <td>2 5</td> <td>3</td> <td>a</td> <td>3</td> <td>2</td> <td>1 0 0</td> <td>66</td> <td>00 00</td> <td>63</td> <td>65</td> <td>88</td> <td>79</td> <td>75</td>	*	Cimilar	SIMILIZ	90	66	98	100	100	99	1	5	8	57	5	100	92	55	100	5	100	5	66	5	88	9	91	11	83	9	73	100	95	100	8	2	65	9	3	30	2 5	3	a	3	2	1 0 0	66	00 00	63	65	88	79	75
Family         Group         nraa         Length Latch         ID           AGC         GRK         2.76-314         68         637           AGC         GRK         1.30E-180         378         371           AGC         GRK         1.30E-180         378         371           AGC         GRK         1.30E-180         378         371           AGC         GRC         1.30E-180         378         371           AGC         GAGLI I. ce         1.46E-137         414         424           AGC         GAGLI I. ce         1.0E-10         729         729           AGC         NDR         1.30E-18         88         42           AGC         NDR         1.0E-10         105         42           AGC         NDR         1.0E-10         105         42           AGC         NDR         6.10E-181         464         483           AGC         PKC         1.0E-10         105         42           AGC         PKC         1.0E-10         105         42           AGC         SGK         2.0E-15         489         489           AGC         SGK         2.0E-16         349	*	-	-	<del>6</del>	88	71	100	100	46	69	5	67	42	9	5	100	38	<b>5</b> 0	<b>100</b>	100	8	66	6	88	9	33	65	67	44	55	100	91	9	8	5	94	6	3	3 5	2 5	3 :	6	3	8	100 100	66	100	41	53	57	62	29
AGC         GRAK         1.30E-180           AGC         GRK         1.30E-181           AGC         NDR         1.30E-181           AGC         NDR         1.30E-181           AGC         NDR         1.0E-10           AGC         NDR         1.0E-10           AGC         PKC         1.0E-10           AGC         SGK         2.90E-15           AGC         SGK         2.90E-16           CAMK         CAMK         1.0E-21           CAMK         CAMK         1.0E-11           CAMK         CAMK         1.0E-21           CAMK         CAMK         1.0E-21           CAMK         EMK         1.0E-21           CAMK	match	+	1	687	371	262	414	729	73	42	483	915	42	980	889	204	94	469	745	549	430	426	244	375	349	89	468	199	181	147	372	340	414	1053	153	122	729	462	657	200	25	è	2	211	2227	67	1284	114	181	188	138	146
AGC         GRAK         1.30E-180           AGC         GRK         1.30E-181           AGC         NDR         1.30E-181           AGC         NDR         1.30E-181           AGC         NDR         1.0E-10           AGC         NDR         1.0E-10           AGC         PKC         1.0E-10           AGC         SGK         2.90E-15           AGC         SGK         2.90E-16           CAMK         CAMK         1.0E-21           CAMK         CAMK         1.0E-11           CAMK         CAMK         1.0E-21           CAMK         CAMK         1.0E-21           CAMK         EMK         1.0E-21           CAMK	Lenoth	. A.	g	688	378	419	414	729	329	88	464	978	105	890	889	205	384	469	745	549	431	430	244	446	349	440	669	297	708	909	372	372	414	1311	438	438	729	462	1330	200	076	670	3	874	2286	127	1287	514	508	478	266	247
Family  AGC  AGC  AGC  AGC  AGC  AGC  AGC  AG	†	t	Pscore	2.7e-314	1.30E-190				1.20E-09	1.30E-19	6.10E-181	8.60E-160	1.10E-10	0	9.46-319	1.20E-106	3.60E-12	2.90E-257	7.00E-178	9.60E-222	9.20E-103	2.90E-157	2.00E-76	4.10E-211	5.60E-216	1.40E-19	1.50E-165	1.60E-62	2.60E-48	2.60E-31	3.10E-121	7.90E-93	1.20E-113	5.90E-185	1.20E-45	1.40E-32	1.30E-184	3.50E-126	0 101 2	9.00C 444	3.00C-111	/.30E-80	1.40E-244	8.20E-76	0	7.80E-37	0	5.00E-20	3.30E-89	8.60E-98	9.60E-39	7.10E-48
		21.0.3	Group	GRK	GRK	03C11.1_ce	03C11.1_ce	03C11.1 ce	NDR	NOR	NOR	PKC	PKC	PKC	PKC	PKC	S6K	SeK	Sex	S6K	SGK	SGK	SGK	SGK	A6	AMPK	CAMK	CAMK	CAMK	CAMK	DAPK	DAPK	DAPK	EMK	EMK	EMX	EMK	EMK	TIME S	LIMIL	LIMI	T T T	TWA	<b>M</b> CK	Trio	Trio	Trio		i i	ı	ı	
Seq         Seq           Seq         Seq           Seq         Seq           Seq         Seq           Seq         Seq           102         122           122         123           124         125           127         128           128         127           129         130           131         131           141         135           131         141           22         141           23         144           24         144           27         141           28         144           29         140           20         141           21         145           22         146           23         150           33         153           34         154           35         155           36         156           37         157           38         156           44         161           45         166           46         166           46         166		Camille	ramily	AGC	AGC	AGC	AGC	AGC	AGC	AGC	AGC	AGC	AGC	AGC	AGC	AGC	AGC	AGC	AGC	AGC	AGC	AGC	AGC	AGC	Atypical	CAMK	CAMK	CAMK	CAMK	CAMK	CAMK	CAMK	CAMK	CAMK	CAMK	CAMK	CAMK	CAMK	CAMK		S S S	CAMIK	CAMK	CAMK	CAMK	CAMK	CAMK	CAMK	중	ક	CMGC	CMGC
10.5         10.5 <td< td=""><td>Sea</td><td></td><td>aa Dii</td><td>122</td><td>123</td><td>124</td><td>125</td><td>126</td><td>127</td><td>128</td><td>129</td><td>130</td><td>131</td><td>132</td><td>133</td><td>134</td><td>135</td><td>136</td><td>137</td><td>138</td><td>139</td><td>140</td><td>141</td><td>142</td><td>143</td><td>144</td><td>145</td><td>146</td><td>147</td><td>148</td><td>149</td><td>150</td><td>151</td><td>152</td><td>153</td><td>153</td><td>154</td><td>3</td><td>8</td><td>200</td><td>8</td><td>Ž į</td><td>3</td><td>9</td><td>162</td><td><u>8</u></td><td>164</td><td>165</td><td>166</td><td>167</td><td>168</td><td>169</td></td<>	Sea		aa Dii	122	123	124	125	126	127	128	129	130	131	132	133	134	135	136	137	138	139	140	141	142	143	144	145	146	147	148	149	150	151	152	153	153	154	3	8	200	8	Ž į	3	9	162	<u>8</u>	164	165	166	167	168	169
	Sed	300	U# 11a	-	7	9	4	S	9	_	80	6	9	=	12	13	14	5	16	17	9	19	02	21	22	23	24	52	82		58	30	31	35	33	33		4	8		1	3	5	4	42				1 1	. !	1 48	

|  | Ţ.   | Т  | ī   | 1   | Γ  |  | <u> </u>  | Г   |   
   
   
   
   
   
   | Ī   | 1  | 1   | i  
  | !  
   
   
   
   
   | :  | Г   | ī   | 1  | ,   
   | 1  | 1   | . ;  | -1  | 7   | -   
  | !  
   
   
  | -  
  | -   | ŗ  | 1   | 1  | -   | -;-  
   | -;-   | :   |  | -  | į  | ,   |                                    
   |  |  | -  |  |   
  | _   | _  |
|--|--|--|---|---|--|--|---|---
--
--
--
--
--
--
-------------------------------------|---|--|---|---
--
--
--
--
--
--|--|---|---|--
---|--|---|--|---|---
--
--
--
--
---|---
---	--	---	--	---
--	---	--	--	--
--	--	--	---	--
261	261	261	261	261
   
   
   
   
   
   | 261   | 261  | 281   | 261  
  | 261  
   
   
   
   
   | 797  | 281   | 261   | 261  | 281   
   | 261  | 261   | 147  | 147   | 781   | 197   
  | 38   
   
   
  | 261  
  | 128   | 261  | 261   | 261  | 202   | 2  
   | 118   | 143   | 261  | 261  | 261  | 261   | 261                                
   | 261  | 261  | 261  | 261  | 9   
  | ē   | 5  |
| -  | -  | 235  | 134   | -   | 1  | -  | -   | -   | 65  
   
   
   
   
   
   | -   | 235  | -   | -  
  | 85   
   
   
   
   
   | -  | -   | -   | -  | 235   
   | -  | -   | 65   | 116   | -   | £ .   
  | -  
   
   
  | -  
  | 101   | -  | -   | -  | E 5   | 8  
   | 47  | 2   | -  | -  | -  | -   | -                                  
   | -  | 7  | -  | - -  | - -   
  | - .   | - ;  |
| 1020   | 385  | 28   | 153   | 493   | 305  | 285  | 284   | 364   | 187   
   
   
   
   
   
   | 267   | 86   | 479   | 327  
  | 170  
   
   
   
   
   | 446  | 285   | 527   | 487  | 103   
   | 539 & 1001   | 583   | 187  | 150   | 200   | 222   
  | 318  
   
   
  | 266  
  | 39  | 259  | 723   | 620  | 77  | 227  
   | 131   | 305   | 531  | 265  | 265  | 280   | 272                                
   | 267  | 213  | 329  | 408  | 340   
  | 200   | 607  |
| 21   | 4  | -  | -   | 177   | 5  | 4  | 4   | 109   | 101   
   
   
   
   
   
   | 7   | 29   | 221   | 73   
  | -  
   
   
   
   
   | 165  | 24  | 199   | 174  | 76  
   | 80 & 590   | 167   | 5  | 91.5  | 6 -   | 518   
  | 3  
   
   
  | 12   
  | 12  | 16   | 463   | 357  | - 5   | 3 6  
   | 88  | 230   | 79   | 9  | 2  | 25  | 12                                 
   | 12   | -  | -  | 80.  | 25  
  | ,   |  |
| CDC2-related protein kinase 7 [Homo sapiens] | NKIAMRE [Homo saplens]   | NKIATRE alpha (Rattus norvegicus)  | Cell cycle related kinase [Homo sapiens]  | Cyclin-dependent kinase-like 1 (CDC2-related kinase) [Homo sa   | Extracellular signal-regulated kinase 7; ERK7 [Rattus norvegicus   | Renal tumor antigen [Homo sapiens]   | intestinal cell kinase [Homo sapiens]   | MLCK (Rattus norvegicus)  | CG10873 gene product [Drosophila melanogaster]  
   
   
   
   
   
   | Hypothetical protein [Homo sapiens]   | Hypothetical protein [Homo sapiens]  | KIAA0344 gene product [Homo sapiens]  | Nuclear receptor binding protein [Homo saplens]  
  | Nuclear receptor binding protein [Homo sapiens]  
   
   
   
   
   | Ca2+/calmodulin-dependent protein kinase kinase beta [Homo s   | Hypothetical 33.6K protein - rabbit fibroma virus   | Nuclear body associated kinase 1a [Mus musculus]  | Dual-specificity tyrosine-(Y)-phosphorylation regulated kinase 3   | tion regulated kinase 3                           
   |  | CG10873 con a sediction ractor 2-alpha kinase Homo sapiens  | (AE003587) C 10673 gang product in the control of t | Interdeukin, 1 recentor-associated kings M. Lama sanian   | Interdeukin-1 recentor-associated kinase M (Homo emigra)  | fre1, inostot-requiring 1 gene [Mus musculus]   
  | CG8173 gene product [Drosophila melanogaster]  
   
   
  | CG8173 gene product [Drosophila melanogaster]  
  | testis-specific kinase 2 [Homo sapiens]   | Mixed lineage kinase [Homo sapiens]  | Futative protein-tyrosine kinase (Homo sapiens)   | Recentor Inferaction protein 3 (Aug. museulus)   | Hypothetical protein (Homo sapiens)                                   | KIAA1360 protein [Homo sapiens]  
   | CG1973 gene product [Drosophila melanogaster]   | Unnamed protein product [Homo sapiens]  | Serine/threonine kinase 23 [Homo sapiens]  | Serine/threonine kinase 22A (spermiogenesis associated) [Mus   | serine/threonine kinase 22B (spermiogenesis associated)  | Serine/Ihreonine kinase 22A (spermiogenesis associated) | Serine/threonine kinase 228
(spermiogenesis associated) [Mus   | Serine/Inregnine kinase 22A (spermiogenesis associated)  | Detriller in recording kinase 228 (spermiogenesis associated)  | The protein kinase (Arabidopsis thanana)   | UNC-51-like kinase (I.I.K.) 2 (Mis miscalus)                 | Hypothetical protein DKFZp434C131.1 - human (franment)  
  |   | Senim-inducible kinase (Homo capiane)  |
| AAF 36401.1                                  | AAF36509.1   | AAF34871.1   | NP 036251.1   | NP 031740.1   | AAD12/19.1   | A A E 9 7 2 7 4  | PACS/2/0.1  | P20689  | AAF50789.1  
   
   
   
   
   
   | CAB/0864.1  | CAB/0864.1   | NF 033638.1   | NP 037524.1  
  | NP 03/524  
   
   
   
   
   | AAU31507.1   | JQ1743  | AAU32566.1  | NP 0035/3.1  | ND 038747   
   | ND 055228 4  | AAF50799 1  | AAF50799 1   | NP 009130 1   | NP 009130.1   | NP 036146.1   
  | AAF48758.1   
   
   
  | AAF48758.1   
  | NP 009101.1   | AAF 63490.1  | BAA22317 1  | AAF03133.1   | CAB55300.1  | BAA92598.1   
   | AAF56933.1  | BAA91097.1  | NP 055185.1  | NP 033461.1  | NP 033462 1  | NP 033461.1   | NP 033462.1                        
   | NP 033461.1  | AAD32787 4   | BAA77341 1   | BAA77341.1   | T17265  
  | BAA91270.1  | AAD00575 1   |
| <b>2</b>                                     | 82   | 8  | 8   | 60  | 5  | 3 5  | 3;  | 1   | ۵,  
   
   
   
   
   
   | 3 8   | 8  | S.  | 3  
  | 30   
   
   
   
   
   | 3  | 75  | 3 3   | 30   | 8 8   
   | 3 5  | 67  | 99   | 100   | 85  | 89  
  | 62   
   
   
  | 20   
  | 95  | 9  | 3 5   | 8 8  | 9   | 88   
   | 61  | 9   | <u></u>  | 2  | 88   | 8   | 2 2                                
   | 20   | 3 %  | 26   | 26   | 100   
  | 96  | S  |
| 3 5  | 82   | 92   | 28  | 6   | 2  | 3 5  | 3 8   | 3 9   | 9 5   
   
   
   
   
   
   | 3 2   | <b>4</b> 8   | 8 5   | 3 8  
  | 8  
   
   
   
   
   | 3 8  | 3 5   | ) A   | 3 8  | 8 8   
   | 5  | 46  | 45   | 8   | 75  | 82  
  | 45   
   
   
  | 32   
  | 92  | 200  | 3 5   | 8  | 9   | 98   
   | 45  | 8   | <u></u>  | 9 :  | 8 ;  | 5   | 3 4                                
   | 2  | 9  | 37   | 38   | 100   
  | 96  | 69   |
| 1490   | 377  | 225  | 128   | 436   | 2 5  | 632  | 900   | 2 5   | 200   
   
   
   
   
   
   | 86  | 1403   | 536   | 5 5  
  | 7/0  
   
   
   
   
   | 90   | 1437  | 200   | 140  | 1493  
   | 630  | 102   | 8  | 596   | 293   | 746   
  | 102  
   
   
  | <u>5</u>   
  | 37  | 56   | 385   | 288  | 688   | 354  
   | 396   | 648   | 533  | 77   | /21  | 717   | 326                                
   | 73   | 57   | 53   | 25   | 247   
  | 468   | 27   |
| 1430   | 224  | 237  | 211   | 688   | 5 2  | 632  | 3 5   | 25.2  | 200   
   
   
   
   
   
   | 3 6   | 1050   | 536   | 27.8   
  | 2 0  
   
   
   
   
   | 8 6  | 12.5  | 663   | 188  | 1649  
   | 630  | 253   | 216  | 596   | 392   | 922   
  | 225  
   
   
  | 280  
  | 4 8   | 2 4  | 634   | 289  | 688   | 505  
   | 808   | 649   | 533  | 8 8  | 20,000   | 787   | 27.6                               
   | 218  | 333  | 412  | 341  | 480   
  | 565   | 39   |
| 0 205 404                                    | 4 40E 101  | 1.40E-128  | 3.00E-68  | 0 10E 80  | 2 30E-180  | 1.50E-180  | 1 ANE.79  | 2 50E-45  | 2.30F.158   
   
   
   
   
   
   | 1 ROE-152   | 8 70F-300  | 1 10F-254   | 2 50E-208  
  | 3 80E-448  
   
   
   
   
   | 0.00E.24   | 0.305-24  | 2 10E.280   | 2.30E-95   | 0   
   | 1.50E-220  | 2.50E-45  | 3.70E-45   | 0   | 1.20E-170   | 1.5e-323  
  | 8.70E-40   
   
   
  | 5.90E-32   
  | 2 50E 202   | 8 ROE-251  | 2.20E-158   | 5.30E-158  | 0   | 1 70E-209  
   | 2.20E-157   | 7.40E-196   | 3.80E-252  | 3.00E-33   | 2.70E-32   | 4.0UE-10  | 2 10F-33                           
   | 2 50F-32   | 0.000062   | 0.002492   | 0.001096   | 1.90E-68  
  | 1.60E-208   | 6.70E-10   |
|  | 5 5  | 333  | ¥ 3   | SC K  | Ş  | ZĞ.  | RCK   | YGR262 er   | C28C2 ce  
   
   
   
   
   
   | C26C2 Ce  | C26C2 ce   | C26C2 ce  | C26C2 Ce   
  | CAMKK  
   
   
   
   
   | CTR1   | DYRK  | OVEK  | OYRK   | EIFK  
   | EFF  | Endop   | Endop  | IRAK  | IRAK  | Æ   
  | KYK2 dd  
   
   
  | KYK2 dd  
  | אווען אווען   | M K  | RP  | RIP  | SCY1 sc   | -  
   | $\rightarrow$   | SLOB?   | CTV  | STUD   | STKOOD   | STK22A  | TSK Y                              
   | TSK  | CNC  | CNC  | S  | S   
  | ONC   | Unique   |
| O C  | O CONT   |  | CMG   | CMGC  | CMGC   | CMGC   | CMGC  | Microbial PK  | Other   
   
   
   
   
   
   | Other   | Other  | Other   | Other  
  | Officer  
   
   
   
   
   | Other  | Other   | Other   | Other  | Other   
   | Other  | Other   | Other  | Other   | Other   | Other   
  | of per   
   
   
  | Ciner  
  | S S   | Other  | Other   | Other  | Other   | Other  
   | Glie  | ie C  | o de la  |  | o de   | o libe  | Other                              
   | Other  | Other  | Other  | Other  | Other   
  | Other   | Other  |
| 172  | 173  | 174  | 175   | 176   | 177  | 178  | 179   | 180   | 181   
   
   
   
   
   
   | 182   | 183  | 184   | 185  
  | 186  
   
   
   
   
   | 187  | 188   | 189   | 180  | 191   
   | 192  | 193   | 194  | 195   | 186   | 197   
  | 198  
   
   
  | A C  
  | 3 5   | 202  | 203   | 204  | 205   | 506  
   | /07   | 8 8   | 210  | 2  | 212  | 213   | 214                                
   | 215  | 218  | 217  | 218  | 219   
  | 220   | 221  |
| 2  | 3 8  | 3 2  | 5   | 28  | 57   | 28   | 29  | 8   | 150   
   
   
   
   
   
   | 8   | 83   | 25  | 89   
  | 99   
   
   
   
   
   | 6  | 89  | 69  | 2  | 7.  
   | 73   | 74  | 22   | 92  | =   | 2   
  | 2  
   
   
  | 2  
  | 8   | 83   | 84  | 82   | 88  | 87   
   | 8   | 8 8   | 8 2  | 3  | : 2  | 8   | 98                                 
   | 96   | 97   | 98   | 66   | 9   
  | 힐   | <u>2</u>   |
|  | 172 CMSC CRIS 1.10C-20-1 149U 10U AAI-38401.1 CDCZ-related protein kinase 7 [Homo saplens] 21 1020 1 | 172 CMGC CDK 9.20E-101 534 377 82 82 AAF38509.1 NKIAMRE [Homo saplens] 21 1020 1 | 172         CMGC         CDK         9.20E-101         534         377         82         82         AAF38509.1         NKIAMRE [Homo saplens]         4         385         1           173         CMGC         CDK         1.40E-128         337         225         92         96         AAF34871.1         NKIATRE alpha [Rattus norvegleus]         1         28         235 | 172         CMGC         CDK         9.20E-101         534         377         4850-609.1         1000         AAP36401.1         CDCZ-related protein kinase 7 (Homo sapliens)         21         1020         1           173         CMGC         CDK         9.20E-101         534         377         225         82         AAF36509.1         NIKIAMRE [Homo sapliens]         4         385         1           174         CMGC         CDK         1.40E-128         337         225         82         86         AAF34671.1         NIKIAMRE [Homo sapliens]         1         28         235           174         CMGC         CDK         3.00E-86         211         159         79         84         NP 039251.1         Cell bycle related kinase [Homo sapliens]         1         153         134 | 172         CMGC         CDK         1.0E-224         137         100         AAF3849.1.         CMCZ-felated protein kinase 7 (Homo saplens)         21         1020         1           173         CMGC         CDK         9.20E-101         534         377         285         92         AAF3859.1         NKIAMRE Homo saplens)         4         385         1           173         CMGC         CDK         1.40E-128         337         225         92         AAF3857.1.1         NKIAMRE Homo saplens         4         385         1           174         CMGC         CDK         3.00E-88         211         159         79         84         NP 036251.1         Cell cycle related kinase Homo saplens         1         153         134           175         CMGC         CLK         1.50E-242         499         436         91         93         NP 031740.1         Cyclin-dependent kinase-like I (CDC2-related kinase) [Homo saplens]         1         153         134           175         CMGC         CLK         1.50E-242         499         93         NP 031740.1         Cyclin-dependent kinase-like I (CDC2-related kinase) [Homo saplens]         1         154 | 172         CMGC         CDK         1.05-242         1450         100         AAF36509.1         NKIAMRE Honous saplens]         21         1020         1           173         CMGC         CDK         9.20E-101         137         82         82         82         86         AAF36509.1         NKIAMRE Honous saplens]         4         385         1           174         CMGC         CDK         1.40E-128         337         225         82         86         AAF3487.1         NKIAMRE Honous saplens]         1         1         28         235           174         CMGC         CDK         3.00E-88         2.11         159         79         84         NP 034740.1         Cell cycle related kinase Homo saplens]         1         153         134           175         CMGC         CLK         1.50E-242         499         436         91         93         NP 031740.1         Cyclin-dependent kinase-like i (CDC2-related kinase) [Homo sa 177         493         1           176         CMGC         RCK         9.10E-89         544         AAD4012719.1         Extracellular signal-regulated kinase 7. ERK7 [Rattus norvegicus]         1         1         1 | 172         CMGC         CDK         9.20E-101         130         AAP 36401.1         CDCZ-felated protein kinase 7 (Homo saplens)         21         1020         1           173         CMGC         CDK         9.20E-108         337         225         82         AAF 36509.1         NKIAMRE Homo saplens)         4         385         1           174         CMGC         CDK         1.40E-128         337         225         82         84         AN 0 3651.1         Cell selbra (Rattus noveglous)         1         1         28         235           175         CMGC         CLK         1.50E-242         499         436         91         83         NP 031740.1         Cellegendent kinase-like 1 (CDC2-related kinase) [Homo saplens]         1         153         13           176         CMGC         RCK         2.30E-189         544         343         57         64         AAD12719.1         Extracellular signal-regulated kinase 7; ERK7 [Rattus norveglous 13         305         1           177         CMGC         RCK         2.30E-189         419         100         100         NP 03544.1         Renal lumor antigen (Homo saplens)         4         285         1 | 172         CMGC         CDK         9.20E-104         135         100         AAP36401.         CDCZ-felated protein kinase 7 [Homo saplens]         21         1020         1           173         CMGC         CDK         9.20E-108         337         82         AAF36509.1         NKIAMRE [Homo saplens]         4         335         1           174         CMGC         CDK         3.00E-88         211         159         78         84         NP 036251.1         Cell Cycle related kinase [Homo saplens]         1         28         235           175         CMGC         CLK         1.50E-242         499         436         91         83         NP 031740.1         Cell Cycle related kinase [Homo saplens]         1         134         134           176         CMGC         CLK         1.50E-189         544         343         57         64         AAD12719.1         Extracellular signal-regulared kinase [Homo saplens]         4         285         1           177         CMGC         RCK         2.30E-189         419         100         100         NP 055041.1         Renal lumor antigen [Homo saplens]         4         286         1           179         CMGC         RCK         2.50E-189         419 | 172         CMGC         CDK         9.20E-101         534         377         AAF38509 In CUC2-telated protein kinase 7 [Homo saptens]         21         1020         1           173         CMGC         CDK         1.40E-128         337         225         82         82         86         AAF38509 In KIMAMRE [Homo saptens]         4         385         1           174         CMGC         CDK         1.40E-128         337         225         82         86         AAF34871.1         INKIAMRE [Homo saptens]         1         28         235           175         CMGC         CDK         1.30E-242         499         436         91         84         NP 039251.1         Cell cycle related kinase [Homo saptens]         1         153         134           175         CMGC         CLK         1.0E-242         499         436         91         83         NP 031740.1         Cyclin-dependent kinase [Homo saptens]         177         493         1           175         CMGC         RCK         9.10E-89         544         419         100         NP 031740.1         Cyclin-dependent kinase [Homo saptens]         13         305         1           176         CMGC         RCK         1.50E-189         419 <td>172         CMGC         CDK         1.0E-24         377         AAF36509.1         NIXIAMRE Hono saplens]         21         1020         1           173         CMGC         CDK         9.20E-101         534         377         225         82         AAF36509.1         NIXIAMRE Hono saplens]         4         385         1           174         CMGC         CDK         1.40E-128         337         225         82         86         AAF34871.1         NIXIAMRE Hono saplens]         1         28         235         1           175         CMGC         CDK         1.00E-88         211         159         79         84         NP 036251.1         Cell Cycle related kinase Homo saplens]         1         153         134           175         CMGC         CLK         1.50E-242         499         436         91         83         NP 031740.1         Cell Cycle related kinase Homo saplens]         1         153         134           176         CMGC         CLK         1.50E-249         419         419         100         NP 031740.1         Cell Cycle related kinase Homo saplens]         1         4         285         1           177         CMGC         RCK         2.30E-189         4</td> <td>172         CMGC         CDK         9.20E-101         534         377         82         AAF36509.1         NIXIAMRE Homo saplens]         21         1020         1           173         CMGC         CDK         9.20E-101         534         377         82         82         AAF36509.1         NIXIAMRE Homo saplens]         4         385         1           174         CMGC         CDK         3.00E-88         2.11         159         79         84         NP 036251.1         Cell cycle related kinase Homo saplens]         1         153         13           175         CMGC         CLK         1.50E-242         499         436         91         83         NP 031740.1         Cyclin-dependent kinase Homo saplens]         1         153         13           176         CMGC         RCK         9.10E-89         544         343         57         64         AAD1278.1         Extracellular signal-regulated kinase I/Formo saplens]         4         285         1           177         CMGC         RCK         1.50E-180         632         610         100         NP 05504.1         Renal lumor anilgan Homo saplens]         4         286         1           178         CMGC         RCK         1.50E</td> <td>172         CMGC         CDK         9.20E-101         534         377         82         AAF36509.1         NKIAMRE Home saplens]         21         1020         1           173         CMGC         CDK  
      9.20E-101         534         377         82         AAF36509.1         NKIAMRE Home saplens]         4         385         1           173         CMGC         CDK         1.00E-88         211         159         79         84         NP 03651.1         Cell byte related kinase Home saplens]         1         153         135           174         CMGC         CLK         1.0E-242         499         436         91         83         NP 031740.1         Cyclin-dependent kinase-like i (CDC2-related kinase) [Home saplens]         1         153         13           175         CMGC         RCK         2.30E-189         544         343         57         64         AAD12781.1         Renal kinase Home saplens]         1         17         493         1           176         CMGC         RCK         1.30E-189         419         100         100         NP 05504.1         Renal kinase Home saplens]         4         285         1           178         CMGC         RCK         1.00E-79</td> <td>172         CMGC         CDK         9.20E-104         130         AAP 3640.1         CDCZ-felated protein kinase 7 [Homo saplens]         21         1020         1           172         CMGC         CDK         9.20E-104         134         37         225         82         AAF 36509.1         NKIAMRE [Homo saplens]         4         385         1           173         CMGC         CDK         1.40E-128         337         225         82         84         NP 03651.1         Cell elated kinase Homo saplens]         1         153         134           175         CMGC         CLK         1.50E-242         499         436         91         83         NP 031740.1         Cyclin-dependent kinase Homo saplens]         1         153         134           176         CMGC         CLK         1.50E-189         544         343         57         64         AAD12719.1         Extracellular signal-regulated kinase 7. ERK7 [Rattus norvegicus]         13         134           176         CMGC         RCK         1.30E-189         544         343         57         64         AAD12719.1         Extracellular signal-regulated kinase 7. ERK7 [Rattus norvegicus]         13         14         286         1           178         CMGC&lt;</td> <td>172         CMGC         CDK         9.20E-101         534         377         0.00         AAP-36401.1         CDCZ-related protein kinase 7 [Homo saplens]         21         1020         1           173         CMGC         CDK         1.40E-128         337         225         82         86         AAF-36501.1         MKIAMRE [Homo saplens]         4         385         1           174         CMGC         CDK         1.40E-128         337         225         82         86         AAF-34671.1         MKIAMRE [Homo saplens]         1         28         235         134           175         CMGC         CDK         1.00E-342         499         436         91         84         NP 039740.1         Cyclin-dependent kinase Plomo saplens]         1         134         134         144         149         100         NP 035741.1         Ratacellular signal-regulated kinase Plomo saplens]         1         28         17         4         285         1         134         17         4         285         1         134         1         14         14         149         100         NP 035741.1         Retacellular signal-regulated kinase Plomo saplens]         1         28         17         4         286         1         <td< td=""><td>172         CMGC         CDK         9.20E-101         5.34         375         100         AAP 58590.1         CLCZ-related protein kinase 7 (Homo saplens)         21         1020         1           173         CMGC         CDK         1.0E-128         337         225         82         86         AAF 38590.1         NIXIAMRE [Homo saplens]         4         385         1           174         CMGC         CDK         1.0E-128         337         225         82         86         AAF 3457.1         I/MINIAMRE [Homo saplens]         1         28         238           175         CMGC         CDK         3.0E-88         211         159         79         84         NP 03625.1         Cell Cycle related kinase [Homo saplens]         1         28         238           175         CMGC         CLK         1.0E-242         49         43         50         64         AAD 12719.1         Extracellular signal-regulated kinase 7: ERK7 [Ratus novegicus]         17         493         1           176         CMGC         RCK         1.50E-189         413         18         60         77         AF 50789.1         Renat lumor anilgan [Homo saplens]         10         10         AAF 50789.1         Renat lumor anilgan [Homo saplens]</td><td>172         CMGC         CDK         1.0E-204         1.35         1.00         AAP 36401.1         CDCZ-felated protein kinase 7 [Homo saplens]         21         1020         1           173         CMGC         CDK         9.20E-101         5.37         2.25         82         AAF 3650.1         NIXIAMRE [Homo saplens]         4         385         1           174         CMGC         CDK         1.0E-128         3.37         2.25         82         AAF 3647.1         INXIAMRE [Homo saplens]         1         28         2.35           175         CMGC         CDK         3.00E-88         2.11         1.39         7.9         84         NP 031740.1         Cell Cycle related kinase Plomo saplens]         1         1.35         1.34</td><td>172         CMGC         CDK         3.00         AAF 38590 1         ICDC2-related protein kinase 7 (Homo sapiens)         21         1020         1           173         CMGC         CDK         1.40E-128         337         225         92         AAF 38591 1         IKIAMRE (Homo sapiens)         1         2         1         120         1           173         CMGC         CDK         1.40E-128         337         225         92         AAF 3467.1         IKIAMRE alpha (Rattus norvegicus)         1         2         2         134           174         CMGC         CLK         1.50E-89         211         159         79         84         NP 03251.1         IKIAMRE alpha (Rattus norvegicus)         1         1         23         134</td><td>172         CMGC         CDK         1.00E-204         1.00E-204</td><td>  172 CMGC CDK   9.20E-24   439   430   140   100   447-385091   MKIAMRE Related protein kinase 7 (Horno saplens)   21   1020   1  </td><td>17.2         CMGC         CDK         3.0E-1021         439         170         ARF36509.1         INMANRE Promo saplens]         21         1020         1           17.2         CMGC         CDK         1.0E-128         337         225         92         96         AAF36509.1         INMANRE Promo saplens]         4         385         21           17.3         CMGC         CDK         1.0E-128         337         225         92         96         AAF36509.1         INMANRE Promo saplens]         1         28         235           17.4         CMGC         CDK         1.0E-246         459         91         84         NP 03140.1         INMANRE Promo saplens]         1         153      
  134           17.5         CMGC         CLK         9.10E-89         544         343         57         64         AAD12718.1         Excepted Raise Plomo saplens]         17         AGD12718.1         Excepted Raise Plomo saplens]         17         AGD12718.1         Excepted Raise Plomo saplens]         17         AGD12718.1         Excepted Raise Plomo saplens]         17         42         285         1           17.6         CMGC         RCK         2.0E-18         419         410         10         NP 03140.1</td><td>17.2         CMGC         CDK         CDK         CDK         CDK         1.00         AAF36509.1         INKIANRE Homo saplens]         21         1.020         1           17.2         CMGC         CDK         1.40E-128         337         225         82         96         AAF36509.1         INKIANRE Homo saplens]         1         2.8         28         235         1.34         3.9         1         33         2.25         82         96         AAF36509.1         INKIANRE Homo saplens]         1         1.53         1.34         3.9         1         3.9         1         1.34         3.9         1         3.3         1.34         3.9         3.0</td><td>172         CMGC         CDK         1.00 C Local         4 30 C Local         1 102 C</td><td>17.2         CMGC         CDK         9.00E-101         13.9         14.0         14.0         Advisional Market Remonsablens         21         10.20         1           11.2         CMGC         CDK         9.00E-101         337         37         Advisional Interval Remonsable Interval Rem</td><td>172         CMGC         CDK         1.00         1.00         APP 38509.1         INIMARIE Home saplens         21         1020         1.0         1.00         1.00         APP 38509.1         INIMARIE Home saplens         1         28         235         1.0</td><td>172         CMGC         CDK         9 20E-101         534         179         170         APF38509 1         INKIAMRE Hone speliens         171         CDKG         CDK         172         CAKG         CDK         173         CAKG         CDK         174         CAKG         CCK         2 30E-38         2 41         317.40         CAKG         CCK         2 30E-38         3 41         3 10         3 10         3 10         3 10         3 10         3 10         3 10         3 10         3 10         3 10         3 10         3 10         3 10         3 10         3 10         3 10         4 10         3 10         3 10         4 10         3 10</td><td>17.2         CMGC         CDK         CDK<!--</td--><td>  172   CMSC   CDK   176E-124   179   170</td><td>  172   CMGC   CDK   1762-124   1759   1750
  1750   1750</td><td>  172   CNIGG   COKA   1.156.20   1.15   1.1</td><td>  172   CMCC   CDK   STREET   STA   /td><td>  CHANGE CON   2.00E-100   334   377   378   379   370</td><td>  172 CMGC CDK   220E-101 534 377 87 87 87 87 87 87 87 87 87 87 87 87 8</td><td>  172 CMSCC CDK   1.005   1.00</td><td>  172 CMGC COR   2.156E-109   179   170  </td><td>17.2         CHACC         CORK         CEACH         CORK         &lt;</td><td>  172   CHAGG   CON.   1.056   1.02
  1.02  </td><td>  172   CHORG   CODK   10.05   1.05  </td><td>  17.2 CHANG CORN   6785-610-1   12-25</td><td>  172 CHIGG CON</td><td>  172 CHOSC CORN   2016   2017   2019</td><td>  17.2   CHOIGE COIN   STATE   /td><td>  17.2   CHOIGG   COCK   STRIET   STRIE</td><td>  17.2 CHOIG CORK 1066:128   17.2 CHOIG CORK 106</td><td>  172 CHOIGE CORK 10867-101-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-</td><td>  172   CHOICE CORK 1000:120   173   173   174  
174   174  </td><td>  11.2   CHOICG CORN   420E-121   537.5   279.1   120   ANX-20041   AUX-20040   AUX-20040</td><td>  17. CHOICE CDN 1.68E-12 337 278 129 129 120 AAASTANI ALCOCATION SERVING AND ASSANDED ALCOCATION SERVING AND ASSANDED ALCOCATION SERVING AND ASSANDED ALCOCATION SERVING AND ASSANDED ALCOCATION SERVING AND ASSANDED ALCOCATION SERVING AND ASSANDED ALCOCATION SERVING AND ASSANDED ALCOCATION SERVING AND ASSANDED ALCOCATION SERVING AND ASSANDED ALCOCATION SERVING AND ASSANDED AND ASS</td></td></td<></td> | 172         CMGC         CDK         1.0E-24         377         AAF36509.1         NIXIAMRE Hono saplens]         21         1020         1           173         CMGC         CDK         9.20E-101         534         377         225         82         AAF36509.1         NIXIAMRE Hono saplens]         4         385         1           174         CMGC         CDK         1.40E-128         337         225         82         86         AAF34871.1         NIXIAMRE Hono saplens]         1         28         235         1           175         CMGC         CDK         1.00E-88         211         159         79         84         NP 036251.1         Cell Cycle related kinase Homo saplens]         1         153         134           175         CMGC         CLK         1.50E-242         499         436         91         83         NP 031740.1         Cell Cycle related kinase Homo saplens]         1         153         134           176         CMGC         CLK         1.50E-249         419         419         100         NP 031740.1         Cell Cycle related kinase Homo saplens]         1         4         285         1           177         CMGC         RCK         2.30E-189         4 | 172         CMGC         CDK         9.20E-101         534         377         82         AAF36509.1         NIXIAMRE Homo saplens]         21         1020         1           173         CMGC         CDK         9.20E-101         534         377         82         82         AAF36509.1         NIXIAMRE Homo saplens]         4         385         1           174         CMGC         CDK         3.00E-88         2.11         159         79         84         NP 036251.1         Cell cycle related kinase Homo saplens]         1         153         13           175         CMGC         CLK         1.50E-242         499         436         91         83         NP 031740.1         Cyclin-dependent kinase Homo saplens]         1         153         13           176         CMGC         RCK         9.10E-89         544         343         57         64         AAD1278.1         Extracellular signal-regulated kinase I/Formo saplens]         4         285         1           177         CMGC         RCK         1.50E-180         632         610         100         NP 05504.1         Renal lumor anilgan Homo saplens]         4         286         1           178         CMGC         RCK         1.50E | 172         CMGC         CDK         9.20E-101         534         377         82         AAF36509.1         NKIAMRE Home saplens]         21         1020         1           173         CMGC         CDK         9.20E-101         534         377         82         AAF36509.1         NKIAMRE Home saplens]         4         385         1           173         CMGC         CDK         1.00E-88         211         159         79         84         NP 03651.1         Cell byte related kinase Home saplens]         1         153         135           174         CMGC         CLK         1.0E-242         499         436         91         83         NP 031740.1         Cyclin-dependent kinase-like i (CDC2-related kinase) [Home saplens]         1         153         13           175         CMGC         RCK         2.30E-189         544         343         57         64         AAD12781.1         Renal kinase Home saplens]         1         17         493         1           176         CMGC         RCK         1.30E-189         419         100         100         NP 05504.1         Renal kinase Home saplens]         4         285         1           178         CMGC         RCK         1.00E-79 | 172         CMGC         CDK         9.20E-104         130         AAP 3640.1         CDCZ-felated protein kinase 7 [Homo saplens]         21         1020         1           172         CMGC         CDK         9.20E-104         134         37         225         82         AAF 36509.1         NKIAMRE [Homo saplens]         4         385         1           173         CMGC         CDK         1.40E-128         337         225         82         84         NP 03651.1         Cell elated kinase Homo saplens]         1         153         134           175         CMGC         CLK         1.50E-242         499         436         91         83         NP 031740.1         Cyclin-dependent kinase Homo saplens]         1         153         134           176         CMGC         CLK         1.50E-189         544         343         57         64         AAD12719.1         Extracellular signal-regulated kinase 7. ERK7 [Rattus norvegicus]         13         134           176         CMGC         RCK         1.30E-189         544         343         57         64         AAD12719.1         Extracellular signal-regulated kinase 7. ERK7 [Rattus norvegicus]         13         14         286         1           178         CMGC< | 172         CMGC         CDK         9.20E-101         534         377         0.00         AAP-36401.1         CDCZ-related protein kinase 7 [Homo saplens]         21         1020         1           173         CMGC         CDK         1.40E-128         337         225         82         86         AAF-36501.1         MKIAMRE [Homo saplens]         4         385         1           174         CMGC         CDK         1.40E-128         337         225         82         86         AAF-34671.1         MKIAMRE [Homo saplens]         1         28         235         134           175         CMGC         CDK         1.00E-342         499         436         91         84         NP 039740.1         Cyclin-dependent kinase Plomo saplens]         1         134         134         144         149         100         NP 035741.1         Ratacellular signal-regulated kinase Plomo saplens]         1         28         17         4         285         1         134         17         4         285         1         134         1         14         14         149         100         NP 035741.1         Retacellular signal-regulated kinase Plomo saplens]         1         28         17         4         286         1 <td< td=""><td>172         CMGC         CDK         9.20E-101         5.34         375         100         AAP 58590.1         CLCZ-related protein kinase 7 (Homo saplens)         21         1020         1           173         CMGC         CDK         1.0E-128         337         225         82         86         AAF 38590.1         NIXIAMRE [Homo saplens]         4         385         1           174         CMGC         CDK         1.0E-128         337         225         82         86         AAF 3457.1         I/MINIAMRE [Homo saplens]         1         28         238           175         CMGC         CDK         3.0E-88         211         159         79         84         NP 03625.1         Cell Cycle related kinase [Homo saplens]         1         28         238           175         CMGC         CLK         1.0E-242         49         43         50         64         AAD 12719.1         Extracellular signal-regulated kinase 7: ERK7 [Ratus novegicus]         17         493         1           176         CMGC         RCK         1.50E-189         413         18         60         77         AF 50789.1         Renat lumor anilgan [Homo saplens]         10         10         AAF 50789.1         Renat lumor anilgan [Homo saplens]</td><td>172         CMGC         CDK         1.0E-204         1.35         1.00         AAP 36401.1         CDCZ-felated protein kinase 7 [Homo saplens]         21         1020         1           173         CMGC         CDK         9.20E-101         5.37         2.25        
82         AAF 3650.1         NIXIAMRE [Homo saplens]         4         385         1           174         CMGC         CDK         1.0E-128         3.37         2.25         82         AAF 3647.1         INXIAMRE [Homo saplens]         1         28         2.35           175         CMGC         CDK         3.00E-88         2.11         1.39         7.9         84         NP 031740.1         Cell Cycle related kinase Plomo saplens]         1         1.35         1.34</td><td>172         CMGC         CDK         3.00         AAF 38590 1         ICDC2-related protein kinase 7 (Homo sapiens)         21         1020         1           173         CMGC         CDK         1.40E-128         337         225         92         AAF 38591 1         IKIAMRE (Homo sapiens)         1         2         1         120         1           173         CMGC         CDK         1.40E-128         337         225         92         AAF 3467.1         IKIAMRE alpha (Rattus norvegicus)         1         2         2         134           174         CMGC         CLK         1.50E-89         211         159         79         84         NP 03251.1         IKIAMRE alpha (Rattus norvegicus)         1         1         23         134</td><td>172         CMGC         CDK         1.00E-204         1.00E-204</td><td>  172 CMGC CDK   9.20E-24   439   430   140   100   447-385091   MKIAMRE Related protein kinase 7 (Horno saplens)   21   1020   1  </td><td>17.2         CMGC         CDK         3.0E-1021         439         170         ARF36509.1         INMANRE Promo saplens]         21         1020         1           17.2         CMGC         CDK         1.0E-128         337         225         92         96         AAF36509.1         INMANRE Promo saplens]         4         385         21           17.3         CMGC         CDK         1.0E-128         337         225         92         96         AAF36509.1         INMANRE Promo saplens]         1         28         235           17.4         CMGC         CDK         1.0E-246         459         91         84         NP 03140.1         INMANRE Promo saplens]         1         153         134           17.5         CMGC         CLK         9.10E-89         544         343         57         64         AAD12718.1         Excepted Raise Plomo saplens]         17         AGD12718.1         Excepted Raise Plomo saplens]         17         AGD12718.1         Excepted Raise Plomo saplens]         17         AGD12718.1         Excepted Raise Plomo saplens]         17         42         285         1           17.6         CMGC         RCK         2.0E-18         419         410         10         NP 03140.1</td><td>17.2         CMGC         CDK         CDK         CDK         CDK         1.00         AAF36509.1         INKIANRE Homo saplens]         21         1.020         1           17.2         CMGC         CDK         1.40E-128         337         225         82         96         AAF36509.1         INKIANRE Homo saplens]         1         2.8         28         235         1.34         3.9         1         33         2.25         82         96         AAF36509.1         INKIANRE Homo saplens]         1         1.53         1.34         3.9         1         3.9         1         1.34         3.9         1         3.3         1.34         3.9         3.0</td><td>172         CMGC         CDK         1.00 C Local         4 30 C Local         1 102 C</td><td>17.2         CMGC         CDK         9.00E-101         13.9         14.0         14.0         Advisional Market Remonsablens         21         10.20         1           11.2         CMGC         CDK         9.00E-101         337         37         Advisional Interval Remonsable Interval Rem</td><td>172        
CMGC         CDK         1.00         1.00         APP 38509.1         INIMARIE Home saplens         21         1020         1.0         1.00         1.00         APP 38509.1         INIMARIE Home saplens         1         28         235         1.0</td><td>172         CMGC         CDK         9 20E-101         534         179         170         APF38509 1         INKIAMRE Hone speliens         171         CDKG         CDK         172         CAKG         CDK         173         CAKG         CDK         174         CAKG         CCK         2 30E-38         2 41         317.40         CAKG         CCK         2 30E-38         3 41         3 10         3 10         3 10         3 10         3 10         3 10         3 10         3 10         3 10         3 10         3 10         3 10         3 10         3 10         3 10         3 10         4 10         3 10         3 10         4 10         3 10</td><td>17.2         CMGC         CDK         CDK<!--</td--><td>  172   CMSC   CDK   176E-124   179   170</td><td>  172   CMGC   CDK   1762-124   1759   1750</td><td>  172   CNIGG   COKA   1.156.20   1.15   1.1</td><td>  172   CMCC   CDK   STREET   STA   /td><td>  CHANGE CON   2.00E-100   334   377   378   379   370 
 370   370</td><td>  172 CMGC CDK   220E-101 534 377 87 87 87 87 87 87 87 87 87 87 87 87 8</td><td>  172 CMSCC CDK   1.005   1.00</td><td>  172 CMGC COR   2.156E-109   179   170  </td><td>17.2         CHACC         CORK         CEACH         CORK         &lt;</td><td>  172   CHAGG   CON.   1.056   1.02  </td><td>  172   CHORG   CODK   10.05   1.05  </td><td>  17.2 CHANG CORN   6785-610-1   12-25 
 12-25   12-25</td><td>  172 CHIGG CON</td><td>  172 CHOSC CORN   2016   2017   2019</td><td>  17.2   CHOIGE COIN   STATE   /td><td>  17.2   CHOIGG   COCK   STRIET   STRIE</td><td>  17.2 CHOIG CORK 1066:128   17.2 CHOIG CORK 106</td><td>  172 CHOIGE CORK 10867-101-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-</td><td>  172   CHOICE CORK 1000:120   173   173   174  </td><td>  11.2   CHOICG CORN   420E-121   537.5   279.1   120   ANX-20041   AUX-20040   AUX-20040</td><td>  17. CHOICE CDN 1.68E-12 337 278 129 129 120 AAASTANI ALCOCATION SERVING AND ASSANDED ALCOCATION SERVING AND ASSANDED ALCOCATION SERVING AND ASSANDED ALCOCATION SERVING AND ASSANDED ALCOCATION SERVING AND ASSANDED ALCOCATION SERVING AND ASSANDED ALCOCATION SERVING AND ASSANDED ALCOCATION SERVING AND ASSANDED ALCOCATION SERVING AND ASSANDED ALCOCATION SERVING AND ASSANDED AND ASS</td></td></td<> | 172         CMGC         CDK         9.20E-101         5.34         375         100         AAP 58590.1         CLCZ-related protein kinase 7 (Homo saplens)         21         1020         1           173         CMGC         CDK         1.0E-128         337         225         82         86         AAF 38590.1         NIXIAMRE [Homo saplens]         4         385         1           174         CMGC         CDK         1.0E-128         337         225         82         86         AAF 3457.1         I/MINIAMRE [Homo saplens]         1         28         238           175         CMGC         CDK         3.0E-88         211         159         79         84         NP 03625.1         Cell Cycle related kinase [Homo saplens]         1         28         238           175         CMGC         CLK         1.0E-242         49         43         50         64         AAD 12719.1         Extracellular signal-regulated kinase 7: ERK7 [Ratus novegicus]         17         493         1           176         CMGC         RCK         1.50E-189         413         18         60         77         AF 50789.1         Renat lumor anilgan [Homo saplens]         10         10         AAF 50789.1         Renat lumor anilgan [Homo saplens] | 172         CMGC         CDK         1.0E-204         1.35         1.00         AAP 36401.1         CDCZ-felated protein kinase 7 [Homo saplens]         21         1020         1           173         CMGC         CDK         9.20E-101         5.37         2.25         82         AAF 3650.1         NIXIAMRE [Homo saplens]         4         385         1           174         CMGC         CDK         1.0E-128         3.37         2.25         82         AAF 3647.1         INXIAMRE [Homo saplens]         1         28         2.35           175         CMGC         CDK         3.00E-88         2.11         1.39         7.9         84         NP 031740.1         Cell Cycle related kinase Plomo saplens]         1         1.35         1.34 | 172         CMGC         CDK         3.00         AAF 38590 1         ICDC2-related protein kinase 7 (Homo sapiens)         21         1020         1           173         CMGC         CDK        
1.40E-128         337         225         92         AAF 38591 1         IKIAMRE (Homo sapiens)         1         2         1         120         1           173         CMGC         CDK         1.40E-128         337         225         92         AAF 3467.1         IKIAMRE alpha (Rattus norvegicus)         1         2         2         134           174         CMGC         CLK         1.50E-89         211         159         79         84         NP 03251.1         IKIAMRE alpha (Rattus norvegicus)         1         1         23         134 | 172         CMGC         CDK         1.00E-204         1.00E-204 | 172 CMGC CDK   9.20E-24   439   430   140   100   447-385091   MKIAMRE Related protein kinase 7 (Horno saplens)   21   1020   1 | 17.2         CMGC         CDK         3.0E-1021         439         170         ARF36509.1         INMANRE Promo saplens]         21         1020         1           17.2         CMGC         CDK         1.0E-128         337         225         92         96         AAF36509.1         INMANRE Promo saplens]         4         385         21           17.3         CMGC         CDK         1.0E-128         337         225         92         96         AAF36509.1         INMANRE Promo saplens]         1         28         235           17.4         CMGC         CDK         1.0E-246         459         91         84         NP 03140.1         INMANRE Promo saplens]         1         153         134           17.5         CMGC         CLK         9.10E-89         544         343         57         64         AAD12718.1         Excepted Raise Plomo saplens]         17         AGD12718.1         Excepted Raise Plomo saplens]         17         AGD12718.1         Excepted Raise Plomo saplens]         17         AGD12718.1         Excepted Raise Plomo saplens]         17         42         285         1           17.6         CMGC         RCK         2.0E-18         419         410         10         NP 03140.1 | 17.2         CMGC         CDK         CDK         CDK         CDK         1.00         AAF36509.1         INKIANRE Homo saplens]         21         1.020         1           17.2         CMGC         CDK         1.40E-128         337         225         82         96         AAF36509.1         INKIANRE Homo saplens]         1         2.8         28         235         1.34         3.9         1         33         2.25         82         96         AAF36509.1         INKIANRE Homo saplens]         1         1.53         1.34         3.9         1         3.9         1         1.34         3.9         1         3.3         1.34         3.9         3.0 | 172         CMGC         CDK         1.00 C Local         4 30 C Local         1 102 C   | 17.2         CMGC         CDK         9.00E-101         13.9         14.0         14.0         Advisional Market Remonsablens         21         10.20         1           11.2         CMGC         CDK         9.00E-101         337         37         Advisional Interval Remonsable Interval Rem | 172         CMGC         CDK         1.00         1.00         APP 38509.1         INIMARIE Home saplens         21         1020         1.0         1.00         1.00         APP 38509.1         INIMARIE Home saplens         1         28         235         1.0    
    1.0         1.0 | 172         CMGC         CDK         9 20E-101         534         179         170         APF38509 1         INKIAMRE Hone speliens         171         CDKG         CDK         172         CAKG         CDK         173         CAKG         CDK         174         CAKG         CCK         2 30E-38         2 41         317.40         CAKG         CCK         2 30E-38         3 41         3 10         3 10         3 10         3 10         3 10         3 10         3 10         3 10         3 10         3 10         3 10         3 10         3 10         3 10         3 10         3 10         4 10         3 10         3 10         4 10         3 10 | 17.2         CMGC         CDK         CDK </td <td>  172   CMSC   CDK   176E-124   179   170</td> <td>  172   CMGC   CDK   1762-124   1759   1750</td> <td>  172   CNIGG   COKA   1.156.20   1.15   1.1</td> <td>  172   CMCC   CDK   STREET   STA   /td> <td>  CHANGE CON   2.00E-100   334   377   378   379   370</td> <td>  172 CMGC CDK   220E-101 534 377 87 87 87 87 87 87 87 87 87 87 87 87 8</td> <td>  172 CMSCC CDK   1.005   1.005   1.005   1.005   1.005   1.005   1.005   1.005   1.005   1.005   1.005   1.005
  1.005   1.00</td> <td>  172 CMGC COR   2.156E-109   179   170  </td> <td>17.2         CHACC         CORK         CEACH         CORK         &lt;</td> <td>  172   CHAGG   CON.   1.056   1.02  </td> <td>  172   CHORG   CODK   10.05   1.05  </td> <td>  17.2 CHANG CORN   6785-610-1   12-25 
 12-25   12-25</td> <td>  172 CHIGG CON</td> <td>  172 CHOSC CORN   2016   2017   2019</td> <td>  17.2   CHOIGE COIN   STATE   /td> <td>  17.2   CHOIGG   COCK   STRIET   STRIE</td> <td>  17.2 CHOIG CORK 1066:128   17.2 CHOIG CORK 106</td> <td>  172 CHOIGE CORK 10867-101-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-</td> <td>  172   CHOICE CORK 1000:120   173   173   174  </td> <td>  11.2   CHOICG CORN   420E-121   537.5   279.1   120   ANX-20041   AUX-20040   AUX-20040</td> <td>  17. CHOICE CDN 1.68E-12 337 278 129 129 120 AAASTANI ALCOCATION SERVING AND ASSANDED ALCOCATION SERVING AND ASSANDED ALCOCATION SERVING AND ASSANDED ALCOCATION SERVING AND ASSANDED ALCOCATION SERVING AND ASSANDED ALCOCATION SERVING AND ASSANDED ALCOCATION SERVING AND ASSANDED ALCOCATION SERVING AND ASSANDED ALCOCATION SERVING AND ASSANDED ALCOCATION SERVING AND ASSANDED AND ASS</td> | 172   CMSC   CDK   176E-124   179   170 | 172   CMGC   CDK   1762-124   1759   1750
  1750 | 172   CNIGG   COKA   1.156.20   1.15   1.1 | 172   CMCC   CDK   STREET   STA   CHANGE CON   2.00E-100   334   377   378   379   370 | 172 CMGC CDK   220E-101 534 377 87 87 87 87 87 87 87 87 87 87 87 87 8 | 172 CMSCC CDK   1.005   1.00 | 172 CMGC COR   2.156E-109   179   170 | 17.2         CHACC         CORK         CEACH         CORK         < | 172   CHAGG   CON.   1.056   1.02  
1.02   1.02 | 172   CHORG   CODK   10.05   1.05 | 17.2 CHANG CORN   6785-610-1   12-25 | 172 CHIGG CON   | 172 CHOSC CORN   2016   2017   2019 | 17.2   CHOIGE COIN   STATE   17.2   CHOIGG   COCK   STRIET   STRIE | 17.2 CHOIG CORK 1066:128   17.2 CHOIG CORK 106 | 172 CHOIGE CORK 10867-101-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1- | 172   CHOICE CORK 1000:120   173   173   174 
 174   174 | 11.2   CHOICG CORN   420E-121   537.5   279.1   120   ANX-20041   AUX-20040   17. CHOICE CDN 1.68E-12 337 278 129 129 120 AAASTANI ALCOCATION SERVING AND ASSANDED ALCOCATION SERVING AND ASSANDED ALCOCATION SERVING AND ASSANDED ALCOCATION SERVING AND ASSANDED ALCOCATION SERVING AND ASSANDED ALCOCATION SERVING AND ASSANDED ALCOCATION SERVING AND ASSANDED ALCOCATION SERVING AND ASSANDED ALCOCATION SERVING AND ASSANDED ALCOCATION SERVING AND ASSANDED AND ASS |

Table 2 (cont'd)

$\overline{}$
$\mathbf{\sigma}$
=
cont
O
Ö
$\tilde{}$
~
0
互
ര

_	_	.,			_								_		,		
88	261	261	7.3	7	136	138	261	281	261	261	38.	261	261	28.	361	261	261
	25	168	4	42	8	8	-	-	-	-	-   α	, -	-	123	-	-	2
159	246	104	272	96	318	78	290	507	251	308	629	002	453	143	292	287	293
80	-	6	-	68	247	7	20	156	4	52	378	449	187	æ	35	4	62
Serine/threonine protein kinase like protein (Arabidopsis thaliana	KiAA1284 protein [Homo sapiens]	Tie gene product [Orosophila melanogaster]	SALIVARY PROLINE-RICH PROTEIN PO (ALLELE K) IHOMO 8	_	Vaccinia related kinase 3 (Homo sapiens)	(AB031052) vaccinia related kinase 3 [Homo sapiens]	MPSK [Homo sapiens]	CG4523 gene product (Drosophila melanogaster)	NEK1 (NIMA-RELATED PROTEIN KINASE 1) IMus musculus	(AC007055) unknown (Homo sapiens)	1	7	(U40827) protein tyrosine kinase (Mus musculus)	-	1	Ι	1 1
CAA18116.1	BAA86578.1	AAF47916.1	P10162	NP 006276.1	BAA90769.1	BAA80769.1	AAC28337.1	AAF46188.1	P51954	AAD31939.1	NP 004663.1	BAA94194.1	AAA98465.1	NP 032036.1	AAF12757.2	NP 036251.1	NP 009101.1
2	45	19	42	25	5	8	5	63	29	98	5	5	8	57	5	ş	100
ន	ຂ	45	ဓ	8	5	82	5	43	48	98	5	5	38	39	5	5	100
8	54	25	25	25	474	191	304	135	122	357	5	719	11	53	367	452	555
349	704	540	240	365	474	234	305	581	969	836	101	719	495	183	367	452	555
0.000022	0.000126	0.007385	0.31334	0.022948	3.10E-263	1.20E-111	7.40E-144	5.10E-49	3.30E-30	2.70E-119	1.10E-291	7.70E-177	4.90E-24	5.30E-18	6.30E-112	2.80E-137	6.50E-233
Unique	Unique	Unique	Unidae	Unique	VRK	VRK	YPL236 sc	YQ09 ce	NEK	NEK	STE11	STE20-02	RTK-20	RTK-20	SGK	CDK	LIMK
Other	Other	Other	Other	Other	Other	Other	Other	Other	STE	STE	STE	·STE	¥	¥	AGC	CMGC	Other
222	223	224	225	228	227	228	229	230	231	232	233	234	235	236	237	238	239
M 103	104	105	108	702	108	109	-	Ξ	115	113	114	115	<u>2</u>	117	118	120	121
-1	-	2	-	-	-	~	<u>+1</u>	<u>+1</u>		_	-	-!	<u>-i</u>	2	-1	<u>+1</u>	_

164 Table 3

These	Yumar-aym	Normal-sym	Yumor - to	Yumor cods	Normal	Endos	p53	SEQ 003	ASEO S YE	# SEQ 806	A 680 000 /	USEQ 9 CA	SEQ 11 EP	SEQ 12 PK	SEO 14 H1	ISFO 16 R
garwnai gland - h Iymph nade - h		1				-		748 815	01 1368	1 58372	7 29848	34709	58988	11606	46820	1316
Down Merow - h		3						446	5 923	6 147758					94839 82024	
merenay gland - h	<b>—</b> —	5					<b>—</b>	96		6 10968	7 4031	4316	1984	1985	24739	290
beucass - y prev -y	<del>                                     </del>	-	<del> </del>		<del> </del>	<del>                                     </del>	-	968							54253 71540	710
carabellum - h		7						6350	1970	4 76722	84606				82436	1279
privatery gland - h	<del> </del>	+	<del> </del>	<del>                                     </del>	<del></del>		<del> </del>	1571	2 768 9 604					11010	87365	1216
piecenta - fi		10						676						13781	103271 80242	1050
fetal kidney - h prostate, h	<del>                                     </del>	11	ļ. — — —			-	<b>—</b>	347					31171	19968	65064	1098
Satel Inver- In		13						330						9454 10418	74934 56577	1116
eathrary pt h		14						272		42976	37947	37758	11433	13806	50763	1440
fetal kang - h sheletal musicio - h	<del> </del>	16	+	<del></del>		├──	┼	518				59484		34594	92518	
heart - It		17						301			27479	20973		11874 11717	57531 43981	778
ernef intestine - h kkiney - h		18			_	_	<b></b>	3920		1 53531	26567	28593	11720	12220	42979	1105
spinel cord - h		20	<del> </del>		<del>                                     </del>	_	<del></del>	5180			1 41491 5 21586		7829 12298	8896 4648	48325 54755	12063 8754
Spiest - h		21 22						375		9 33858	7 34563	16261	11556	8365	40332	8300
Lung - h	<del> </del>	<del>                                     </del>	<del> </del>			-		412					10930	8169 4418	44868 37827	
stomach -N		24						2650	41	31288	33851	12206	5870	3999	18010	7084 5109
testis - h		25	<del>]</del>		<del></del>	-		7654				19148	117943	9866	44850	11194
HPAEC		28				26		7304		5 197406: 0 5866		92648 26274	46509 3919	31139	85252 67087	13780
thyrod gland - h RPTEC		29				30		3870		3 19431	42836	25961	9827	9143	43670	8997
Vaches - N	1	30	<del>                                     </del>			-	<del></del>	24571 6724		3 80360 2 60779		3357 49813	15250	15054	42340 78666	7144
HMEC		32						7791	135	139886	24824	15301	4715	11713	65154	
HCAEC	<del></del>	13 14	<del></del>	<del></del>		<del> </del>	├	5386			34433			15085	66678	8640
Pencrees - h		35						11685	51	4184	19592		1768 6140	28455 6513	\$1717 46443	8203 7564
lymph node - h		36 17				-		6132	73	1 47835	15791	20735	8420	3812	64078	7285
Sheleta muncle - h fetai fiver- h	<u> </u>	38			<del> </del>	╁	$\vdash$	5906			11060	5411 15506	5264 5458	2070 · 2447	30349 56121	3459 9104
Heart - h		39						7091	74	50 15	15303	9552	25151	3920	47672	7275
Duosenum - h	<del></del>	40	<del></del>		<del></del>	-	<del>-</del>	2875		87220	40613	17473		1502	70722	10210
Fetal brain - h		42						12395	336	21478	20505	16311	15818	3563	42191 56960	9323
Salvary gl h		49	$\vdash$		$\vdash$		<u> </u>	4496		5914	17344	12177	4150	3293	35172	8965
HT218-rums			$ldsymbol{ldsymbol{eta}}$		.365	<u> </u>		8962				14956 2191	17932 1738	4389 134	57094 12656	8767
HT213-xomel			=		363		<u> </u>		421	9712	1915	0	144	1080	8245	603
HT 157-normal Ber-13	<del> </del>	<del></del>	<del> </del>		361 356	356	<del></del>	6533			2726	735	12030	854	16328	4100
Bau-12					354	354		11250	128	58750	69954	9439	12012	46921 3467	59687	17604
caraballym - h			<del></del>		344			- 8	242		2939	1746	3951	1243	27729	4240
RPTEC	<del> </del>				334	334	<del>                                     </del>	1977						90571	31402 71803	20777
tyrngin made - h					332			706		1941	7347	7055	14451	1150	30798	8636
h adult SMC 10/21/92 #17 Fetal brain - h	<del></del>	<del></del>	<del> </del> -		330	<u> </u>	<u> </u>	7190						540.	47380	9854
HT396-normal					327			638				10433 320	8848	2972 632	70908 50974	16134 7284
HT149 - normal	<del> </del>				326			6784				10539	7917	2366	70826	13384
HEPM 3d unwented		l	l		320			3252				3937	156 4353	3048	61910	8506 10734
uterus - h					318			4613			39332	19659	31221	6216	66453	15556
thread gland - h			-		316 314		_	4963					10150	4750 6319	46848 44845	11180
advery pl h					311			851	447	161154	19056	6484	8676	1955	51507	13837 11348
prostete, h privatery gland - h			<del> </del>		309 307			1226				5834	8183 4627	1052	47609 34764	10249
pencreas - h					305			193	507			2008 2836	7486	1647	44917	10318
manmary gland - h bladder - h			<b></b>		303			1134				8728	22393	3908	66451	12912
teates - h					298			4247	11127			9508 20243	7386 35776	3929 5632	72421 83198	11960 23260
ibour - h					297			2935	1244	461051	20812	10344	10069	3549	63754	17361
Splean - h apenal cord - h		<del></del>	<del> </del>		296 294	-		55 2252	1587			9704	15258	3701	53225 62962	10529
amail missions - h					292			155	115	366979	12005		6960	1320	41632	13872 4764
etratetal musco - h bone murrow - h			-		290			1375	1462		27541		30044	5272	60372	13925
schwad gland - h					279 277			- 8	918 2174			3118 2570	2421 9223	1687	50557 84753	10424
HPAEC HT392-normal					275	275		501	123	4997	5945	1414	652	1962	37169	7713
HT382-normal			<del> </del>		268 266			253			4487 4938	878	11889	309	38846	3991
Bev-11					239	239		1710	4266	206965	19772	1597	19433	4370	73567	7870 13475
HT372-norms			<del></del>		235 234	235		767	561	52163 34038	6331	1048	7759	6820	50453	7396
Ber 7					233	233			1939	63364	7278	5366 2074	9250	Z350 2698	78267 : 71554 :	14120 9109
Ber-6 Ber-2					231	231		391	2454	49140	7045	5702	6877	2380	52712	9473
8e-1					229	229 227		466 526			9509 6235	799 1909	7032 4847	3425 1045	45448	6479 8089
Station - h					222			329	458	5047	2850	2386	34251	171;	33431	5059
Heart - h stohech -h				-	215	-		682 465		6149	9086	2384 3792	7814 / 15118	1637	45488: 59601;	8442
fetal over- h					213			564	547	5475	5415	1846	1036	4761	39067	10261
PROMOTE - N	-		<del>-</del> -		212	211		522 143	1977		5781 6957	2164 184	9198	1232	43929	9805
fetal brain - h					210			697	3137	52697	9496	7857	14901	1143	70127	8333 12698
PMEC Duccessum - h	<b></b>				209	$\Box$		264	102	5034	5400	0	214;	995	48675	6198
Skeletal muedle - h			<u> </u>		205 203			623			5853	674	1551	579 i	39299	8176 5114
Paricipae - h					201			415	16	56167	5487	3004	4306	891;	33307:	6559
Salvary of + h		-			199	<del> </del>		130 436			2304 4851	2527 Z308	3465 5218	347	26853	4123
HEPM 3d TGFB1 desergent+DName					195			82		4577	2406	Z36	1291	374	21318;	2326
Wi-38 72h	<u> </u>				193	_=		2683	0	247405	21041	4864	19787	2459	33113[	8264
lymph node - h					61			314			16701	4069	4334	2268	21245	1771 4255
tung - h					59	=	=	797	1251	340147	9218j	10510	19588	2388	79535	9151
lidiney - h heart - h					57 55				334 1134	49381 39762		3152	7038 4377	442	\$8006 37503	7384 3564
fessi tung - h					53			0	1323	24481	1809	Z32	1176	1297	12635	3564 1580
fetal inver- h fetal inchey - h			-		51 49			235	37	43001	3182	510	4042	297	21581	2372
HELA-21-031899				79.				277 1376	541 744	37891 109312	3689 5953	2642	11996 5266	3196 1472	31744	4737 6294
HELA-4h-031899 HELA-9h-031899				81				466		171123	4142	2131	6136	5196	\$7302	7191
HELA-0h-031899	<del></del> +			. 83 86				835 646	95	60381 201388	3757 5429	1680	4822	1615	53322	5752
HELA-6h-031899				- 60				1271	164	102436	8381	1801 4751	6490	1222 2346	26774   55350	11015
HELA-8N-031899 HELA-10N-031899				90	$\neg$	=	=	203	410	75136	7198	1647	6591	1636	55168	7319
HELA-11h-031899			+	92 94	<del></del> +			819 D	804		6048 4209	4398 j 312 j	19174	1654	52933 42462	6050 5901
HELA-12h-031899				96					367	43624	9207	1105	6047	885	348251	5882
NCI+G22M NCI-H460				145	<del></del> -		—7	1456 1834	246 168	44456 13945	3419	38703	29485 21487	2702	15500	3126
NCI-H522				150				913	168 254	33641	2979	3669	9837	685	20164	3340 1818
SNB-19 SNB-75				152		=		1115	0	13025	1124	P590	6003	01	16076	2527
SF-268	+		+	154 156	$\overline{}$			1156 231	0	22559 4901	3795 2766	5636 3218	9158 8695	1642	18225	4196 3162
SF-295				158					_342	10978	2136	992	579	648	9339	1613
DU-145	<del></del>	<del></del>	<del></del>	160				1001		18120		5242	2231	416	16835	1694
HCY 116	+			164	+	+		206 721		7942 21002	14891	2626 6955	2690	3599	14305	1886 1853

BNSDOCID: <WO\_\_\_\_0073469A2\_I\_>

165 Table 3 (contd)

The column   1		7	Non-Maria	Turnet - In 1	Turner crafts 1	Normal	Endos	533 I	SEO 003 A	SEO 5 TRIS	SEQ 006 A	SEQ DOS A	SEQ 9 CAR	SEQ 11 EP	SEQ 12 PK	SEQ 14 H1)	SEQ 16 RS
Column	Tissue Ha 578T		nama-ym _	100,00			-		13571	0	186624	34941	16731	12712	9076	46043	5514
The color of the	MCF-7/ADR-RES				+		-		15337	1095	938987	52916	21779	15950	10792	53949	9415
Second Column	M14	149							5452 11456				10734	18346	2544 4588	36000	
Column   C	UACC-257 UACC-62								2455	123	56725	21571	11116	27584	1929	27441.	4551
Table	SK-ME),-28					$\rightarrow$			4479 6387	- 0		13751	7222 8047	23647 23533	4196		8343
	SK-MEL-5	142								690	436888	16465	4434	30762	7048		5242 3132
Column	KM-12 SK-MEL-2								2946	331	331883	16906	13917	13874	7005	30577	5799
The column   The	HCT-15								1187 6598	- 8		18970		21327	5476 8334	45060	
Column   C	COLO 205	137								0	384009	16795	8558	17491	4868	57736	
Column	LOX MIVI	136							11829	0	622856	16554	5952	16514	7213	38849	5702
Second Column	TK-10	134							3536 3482		230533	21155 13660	7532				
1	786-0	132							3264	0	366264	17720	4992	13644	5047	34175	4677
Column   C	HCC-2998	131							9682	177	84811	18456	10359	6438	4663	36960	5785
The color of the	PC-3	129				-			12090	279		14186 21616	7110	11096	3508	35262 40444	6853 5886
The color of the	DU-145	127							16928	138	30590	12131	3150	3840	3261	37777	3307
## 15   10   10   10   10   10   10   10	Cabi-1 Sp	126							3585	257	420391	13247	3620	10151	2543	37859	4327
The color of the	A498	124								0	64349 272936	18090	41974 9419	17229	1191	39104 504651	6293 5958
Column   C	SN12C	122				:			6253	217	203577	17162	14358	29787	5796	32578	5267
Page   Page	HE-60	121				=			4384		440040	12769	10231	15496	2986	28309	4478
Section   Sect	OVCAR-5	119						-		359 798	1086525	16534	5752 8845	41960			9030
Column	OVCAR-4	117							2856	3587	4965335	15528	8040	112397	5681	42598	9203
10	CCRF-CEM		<del></del>						3371	0	551858	10974	7064	21926	5119	52017	5813
19	SF-539	134							4819	0	882870	13841	4718	16963	2604	34565 19576	
MANUAL   11   12   13   14   15   15   15   15   15   15   15	SF-295	112				7			11905	216	68593	15107	8440	7164	2565	40830	7962
Column	ASSIVATEC								3084	1353	233341	16500	6551	11824	2278	30245	3716
Section   Sect	NCI-H522	109				_:		$\vdash$	4147	0	1128364	19715	10185	32962			
Company   Comp	NCLH460	107						$\Box$	6777		452393	13060	6899	18903	4436	28896	5244
Section   1985	SNB-75 NCH-B322M								6471	921	589327	19449	14479	18523	3322	49937	6532
March   Marc	SNB-19	104		F====				$\vdash$		0	219681	17548	1 7956				
1985   1985	SK-OV-J	102							9457	0	202769	15647	7470	11071	2287		2984
Section   Proceedings   Procedings   Proceedings   Procedings   Proceedings   Procee	IGROVI			<del></del>					19803	768	313545	14157	9518	9579	2961	41669	3318
Margan 1976   17   44   10   10   10   10   10   10   10	BCVX	99															
The part of the	HOP-82	97							7908	. 0	317849	22615	4246	39600	3262	33300	3960
													12690	3096	588	30937	5335
March   Marc	h sar sonocytes 2/25/92 #10																5742 6471
March   Marc	A549 - 1								1491	5421	44905	11719	0			0	0
Mart   Mart	A549 - 3	<del> </del>							276	5323					. 0	0	
	A549 - 5																- 0
Form								muteri	846	1343	65024	16784				. 0	
March								mutent	935	934	22597	12511	0		D	0	0
March   Marc							├								- 0		
March   Marc	MCF-7 - 1							wi	840	718	50115	10699	-		0	0	
March   Marc	MCF-7 - 3 MCF-7 - 4			<u> </u>				-	839	1155	140711	14817	1 0		0	0	0
CARPARES	MCF-7 - 5											11019	9				
AGRICAGE	ADR-RES - 1							mutant		3885	51129	18485	9		0	- 0	
Miles		<del>                                       </del>	<u> </u>							951	15870	4445		T		0	
MIN	ADR-RES - 5					┝÷				7502	1292						0
March   Marc	W1 38 - 1							w	619		1182	7 24067					
W 36 : 5		<del> </del>					<u> </u>		642	751	32710	9317			0 0	0	0
Marker	W1 38 - 5							<u> </u>	115	3721	7 6419				0 0		· ō
Section   Sect	HeLo-1								533	12521	1649	3 13319			) 0	0	<u></u>
Main   Main		<u> </u>	<u></u>	<u> </u>				HPV E6	90;	3311	1 4626	788	5		0		0
Martin   M	HeLs - 5			-				HPV E6		1049		§ 9575				0	0
H1290 3	H1299 - 1							mutent	94		6806	7 1472.					
H1299-5	H1298 - 4							mutant	33	2070	7676	9 2935			0	0	0
March   Marc	H1299 - 5			-	<u> </u>	H-			20-	oi	4184	6 1038			0	)! 0	0
Section	A549 · 2			====			<u> </u>	W	19-	4270	3730	7 938	21	) 1			
NCT-116-2	HCT-116 - 1	<del></del>	<u> </u>					w	40	559	7 3933	9134		<u> </u>	0	0	i o
\$F\$59.1   YM	HCT-116 - 2				-	<b>├</b> ──	1	WI mutani	112	375	6 4963 0 4325	1 1382	1	3	31 8	- 0	
\$75.95-7.2   maters   552   317   47973   33235   0   0   0   0   0   0   0   0   0	SF539 · 1	==								1841			5			9	
SF-985-2	SF539 - 2 SF-268-1	<del> </del>	<del></del>	<del></del>		<u> </u>		mutani	56	2 31	7 4285	2 1333	5	:		0	, 0
OFFICE	SF-268-2		F	<b></b>		F		medani	811	9 550	7450	5 1253	3	1			21 0
OVCRR5-1	OVGAR4 - 2							wt	34	2 154	3 10177	7 1042	7	i	)	0 0	0
March   Marc	OVCAR-5 - 1	<del></del>	<del> </del>	<del> </del>			上		16	3] 1	911	0 847	5 (	)	3	0	
ADNI-CES 2   MEV E6   \$16   0   \$12434   \$1374   0   0   0   0   0   0   0   0   0	MCF-7 - 2					<b>—</b>		WE	29	1 143	3 1106	2 768	31 (	)!!			) 0
SW400 - 1   materi   326   0   50775   9762   0   0   0   0   0   0   0   0   0	Hala-2							HPV E6	Sti	В _ (	11243	4 1437	•	)	9	0	0
	SW480 - 1			<del></del>			<u> </u>		108	1 782	6 6813	9 1235	7] (	1		0	
C33  C33	H1299 - 2							mutent	682	3 257:	3 5738	4 1508	11	1	) (		
COCS - 1		<b></b> -	<del></del>	<u> </u>		$\vdash$		mutent	96	115	5 4309	4 1173	2 (	) ]	) (	0 0	0
UKCD - 2	U2OS - 1					=	-		61H	0 8	5 15150	5 1087	2	21			
Maching   5	He68 - 1							w	28	7 59	2 2968	4 1001	1			) 0	0
574   285   8294   116430   0   0   0   0   0   0   0   0   0	He68 - 2 WI 38 - 2	<del></del>			<u> </u>				41	5 247	8 3974	4 2552		· ·	<u> </u>	0	0
Maryan - 3   1956   0   12352   28455   0   0   0   0   0   0   0   0   0						=	=	F	57	4 26	5 829	4 11643	9		0	9	
Machair 4   1996   0   12552   29455   0   0   0   0   0   0   0   0   0							1	4				-, 1003				<u> </u>	· ·
SF72   9430   13002   31583   01   0   0   0   0   0   0   0   0	Methai - 2							_	95	5 69	6 3471	1 3182	91				
MAN 0 15235 13035 0 0 0 0 0	Mechani - 2 Mechani - 3 Mikhail - 4								98 195 75	5 <b>89</b>	5 3471 0 1235 0 847	2 2848 7 27757	3			0	9 0
	Machini - 2 Machini - 3 Machini - 4 Machini - 5 Machini - 5								96 195 75 87	5 89 6 0 943	5 3471 0 1235 0 847 0 1300	2 2848 7 27757 2 3158	3			0 0	0 0

166 Table 3 (contd)

DaPang-7																
Derevo-/	Tumor-sym	Normal-sym	Tumor - 10	Tumor celle	Normal	Endes	p53	SEQ BOX	VEED I TE	BH SEQ GOS	A SEC DOS	A SEQ 9 CA	USEO_11_E	P SEQ 12 P	K 3EQ 14 H	1 5EQ 16 A
DePeng-8	<del> </del>		<del> </del>	+	+	+	₩-	409	1 415	23] 1,3075	1 4800	71	0!	01	2!	0:
DePerg 9			<del> </del>	<del></del>	+ :-	+	+	184		0 12928 2 2313	7 2236					0
DaPeng-11								238		0 5683	6 3435			0		0 ·
DePeng-12 DePeng-10	<del></del>	<del> </del>	+		1		-	162	<u> </u>	0 14341	8 1476	4				o:
Dafferg-1	+	<del></del>	+	+	+	+	+	113	1143							0
DaPang-2				<del></del>		-	<del>                                     </del>	77							3	<u> </u>
DaPeng-3	<del> </del>							103	509	9 6541						0
DePeng-6	<del>                                       </del>	<del>                                     </del>	<del> </del>	+	<del> </del>	+	<del>                                     </del>	1						0 (	i	0
Darwig-6			<del>                                     </del>	+	1 7	+	<del> </del>	175	21	7 3770 0 10425				0 (		0
A549 - 8							wi	14	185							0
EXVX - 8 HCT-116 - 7	<del> </del>				T		COLUMN TO SERVICE MANAGEMENT	26	648	8 7473	2 3417	5 . (	0	0		0
HCT-116 - 8		<del> </del>		+	+	+	w	455		6 6004				Q <u>i</u> (	·	0
HT29 - 1				1		1	materi	293							1	
HT29 - 7 HT29 - 8	<del> </del>		-				arestant.	71			648			0 0		
SF539 - 7	<del></del>			<del> </del>	┿	+	muters wt	181 7384						0 0		
SF539 - 8			<u> </u>					/300					3	0 0		
SF-268-7 SF-268-8							mutent	507	44	5 3305				0 0	-	9:
OVCAR-4 - 7		<del></del>	<del> </del>	+	<del> </del>	+	muteri et	902		0 3010			1	0		01
OVCAR-4 - 8						<del>                                     </del>	=	1384					<del>}</del>	0 0		
OVCAR-5 - 7							mutent		320						<del>}</del>	21 - C
OVCAR-5 - 8 MCF-7 - 8	<del></del>			<u> </u>	<del> </del>	<del>                                     </del>	mutent	156			1096			01 0		01
ADR-RES - B				1	<del> </del>	-	muteri	555 822						o) o		
Hela-8							HPV E6		224			3	<del> </del>	2 0	<del> </del>	?:
SW480 - 7 SW480 - 8	<del> </del>			-		<del></del>	mutent	727					)	3) 0		2, 0
H1299 - 8				-	<del> </del>	+	muteri muteri	226 102	7326			0			i	):
C33A - 7							mutent	372	3126	11403			<del> </del>	0 0		<u> </u>
C33A - 8 U2OS - 7	<del> </del>			+			COLUMN 1		1813	2931	18670	) 0	!!	) 0		
U203 - 7	i		<del></del>	+	<del></del>	<del> </del>	muteri	20 87						0		
Ha68 - 7					1. 1.		w	539	4024	29229		0		0 0		1
Hu68 - 8 WI 38 - 8	<del> </del>			<del> </del>	<del>                                     </del>	<del></del>	3 %	502		71 24757	14259	0		1		
456 medulio RNA					1			232 6548	67			15276	2182	3328		7008
CRL1572 3/17/89						I		110		2070	1153	687	299	1237	25584	
HT368				<del>                                     </del>	<del></del>	84		346 1340	1576			4939	1208	23383	59610	5229
HT378								457	545					916	32554 37558	7666
HT385 HT308	<del></del>			<del> </del>	-			3179					1631	2526	76812	7937
Ber-3					-	173		0 40	390			193		2308 795	21762	8907
Ber-5 Ber-9	$\vdash$			ļ		175		9	420			1068		751	38821 19950	2784
in har eterocytee 2/25/92 #10				<del></del>	<del></del>	177	_	1003	. 0						39076	4356
B=-10					$\overline{}$	237		681	-	93681						5863 7011
HTB10 h fibroblesto 3/31/82 #12	<del></del>							136	0	12913	8\$10	5696	15016	1115	66289	14731
prostate, h					_	<del></del>		\$15 384	37	27263	9059 5219	253 1555	3038		44374	8168
MNNG-OS poly A+								486		280879	11663	2186	10484		29035 24678	
SA-OS (Mundy) poly A+ MK poly A+	<del></del>							1201	0		11068	2632	1909		27097	4279
HCT-116 - 3				<u> </u>			<del>-</del>	1693 420	354 2054	75322 94554	17569 8949	3824	3415		32124	7106
HCT-116 - 4 HCT-116 - 5							w	583		59776	9562	0				- 0
HCT-116 - 6					$\vdash$	$\vdash$	<u></u>	259	377 249		13903					
A549 - 6											12796				0	<u>.                                    </u>
HT29+3 EKVX+8							wi	0	4345	3330	1320			i ol		0
							MILEUM .	302	3771	40888	7326 8815	0	0	0	0	0
HT29 - 4								302 239	3771	40888 \$2593	8615 8637	0	- 8	0	. 0	0
HT29 - 4 HT29 - 5							Mulani Mulani Mulani	302 239 27 448	3771 0 0 1269	68030 25013	8815 8637 9240 18176	0	0	0	0	0
HT29 - 4							Michael Michael Michael Michael Michael	302 239 27 448 309	3771 0 0 1263	40888 \$2593 68030 25013 54935	8815 8637 9240 18176 10000	0000	0	0 0 0	0 0 0 0	0
MT29 - 4 HT29 - 5 HT29 - 6 OVCAR-4 - 3 OVCAR-4 - 4							Mulani Mulani Mulani	302 239 27 448 309 581	3771 0 0 12639 0 1208	40888 \$2593 68030 25013 54935 60523	8815 8637 9240 18176 10000 11477	00000	0 0 0	0 0 0 0	0 0 0 0	0 0 0
MT29 - 4 MT29 - 5 MT29 - 6 OVCAR4 - 3 OVCAR4 - 4 OVCAR4 - 5							Michigani Michig	302 239 27 448 309 581 329 45	3771 0 0 1263 0 1208 487 1926	40888 \$2593 68030 25013 54935 60523 63478 84009	8815 8837 9240 18176 10000 11477 8801 14924	0 0	000000000000000000000000000000000000000	0 0 0 0 0	0 0 0 0	0 0 0 0
MT29 - 4 MT29 - 5 MT29 - 5 OVCAR4 - 3 OVCAR4 - 4 OVCAR4 - 5 CVCAR4 - 5 SF539 - 3							MILEUM MI	302 239 27 448 309 581 329	3771 0 0 12639 0 1208 487 1826 522	40888 \$2593 68030 25013 54923 60523 63478 64009 29081	8815 8637 9240 18176 10000 11477 8801 14924 9741	0 0 0	0 0 0 0 0 0 0	0 0 0 0 0 0	0 0 0 0 0 0 0	0 0 0 0 0
NT29 - 4 MT29 - 5 MT29 - 5 OVCAR4 - 3 OVCAR4 - 4 OVCAR4 - 5 OVCAR4 - 6 SF439 - 3 SF439 - 3							ITELESTIC ITELES	302 239 27 448 309 581 329 45 0 391 408	3771 0 0 12639 0 1208 487 3926 522 0	40888 52593 68030 25013 54925 60523 63478 64009 29981 53862 34224	8815 8637 9240 18176 10000 11477 8801 14924 9741 12881	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0	0 0 0 0 0 0 0	0 0 0 0 0 0	0 0 0 0
MT29 - 4 MT29 - 5 MT29 - 5 OVCAR4 - 3 OVCAR4 - 4 OVCAR4 - 5 CVCAR4 - 5 SF539 - 3							PRICEPT PRICEP	302 239 27 448 309 581 329 45 0 1 391 408	3771 0 0 1259 0 1208 487 3926 522 0 9	60888 \$2593 68030 25013 54035 60522 63478 64009 25981 53652 34254 16367	8815 8637 9240 18176 10000 11477 8801 14924 9741 12881 15917	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0
HT29 - 6 HT29 - 5 HT29 - 6 OVCAR4 - 4 OVCAR4 - 5 OVCAR4 - 6 SF533 - 3 SF533 - 3 SF530 - 6 OVCAR5 - 6							ITELESTIC ITELES	302 239 27 448 309 581 329 45 0 391 408	3771 0 0 12639 0 1208 487 3926 522 0	40888 \$2593 68030 25013 54935 60523 60527 64909 28961 53962 34224 16367 27907	8815 8637 9240 18176 10000 11477 8801 14924 9741 12881 15917 12742 14854	0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0
HT29 - 4 HT29 - 5 HT29 - 5 OVCAR4 - 3 OVCAR4 - 4 OVCAR4 - 5 OVCAR4 - 5 SF533 - 4 SF533 - 4 SF530 - 5 SF530 - 6 OVCAR4 - 3							PRICESSION PRICESSION	302 239 27 448 309 581 329 45 0 391 408 268 0 648	3771 0 0 1253 0 1208 487 3926 522 0 0 1459 617 2513 3066	40888 \$2593 68030 25013 54035 69523 63478 64009 29981 33652 416367 27997 53162 45568	8815 8637 9240 18176 10000 11477 8801 14824 9741 12881 12881 12881 12842 14854 9772 10469	0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0
HT23 - 4 HT23 - 5 HT23 - 5 HT23 - 5 OVCAR4 - 3 OVCAR4 - 3 OVCAR4 - 5 OVCAR4 - 5 OVCAR4 - 5 SESD - 6 OVCAR5 - 3 OVCAR5 - 3 OVCAR5 - 3 OVCAR5 - 3							TRACTORY TRACTORY TRACTORY TRACTORY TRACTORY TRACTORY TRACTORY TRACTORY TRACTORY TRACTORY TRACTORY TRACTORY TRACTORY TRACTORY TRACTORY TRACTORY	302 239 27 448 309 581 329 45 0 291 408 268 0 648	3771 0 0 1269 0 1208 487 3926 522 0 0 1459 817 2513 3066	40888 \$2563 \$25013 \$5935 69523 69523 53476 54079 29881 \$3852 34224 16367 27997 53162 65568 6783	8815 8637 9240 18176 10000 11477 8801 14924 9741 12881 15917 12742 14854 9772 10469 7292	0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
http://display.com/http://displa							TRACTORY TRA	302 239 27 448 309 581 329 45 0 391 408 256 0 648 512 215 711	3771 0 0 1259 0 1208 487 3926 522 0 0 1459 617 2513 3066 444 992 2112	40888 \$2591 86030 25013 54935 69476 69079 29881 53862 77997 53162 45568 6783 19534	8815 8637 9240 18176 10000 11477 8801 14924 17281 12881 13917 12742 14884 9772 10469 7292 7377	0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
HT23 - 4 HT23 - 5 HT23 - 5 HT23 - 5 OVCAR4 - 3 OVCAR4 - 3 OVCAR4 - 5 OVCAR4 - 5 OVCAR4 - 5 SESD - 6 OVCAR5 - 3 OVCAR5 - 3 OVCAR5 - 3 OVCAR5 - 3							mutanti mutanti mutanti mutanti mutanti mutanti mutanti ed ed ed ed ed ed ed ed ed ed ed ed ed	302 239 27 448 309 581 329 45 0 0 391 408 268 0 0 548 751 2215 711	3771 0 0 1259 0 1208 487 3926 522 0 0 1459 617 2513 3066 444 992 2112	40888 \$2590 86030 25013 54035 60523 60523 60523 60523 32981 18367 27997 27997 53162 45560 6783 19534	8815 8637 9240 18776 10000 11477 8801 14924 9741 15917 12242 14864 9772 10469 7729 7292 7377	9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	000000000000000000000000000000000000000
HT29 - 4 HT29 - 5 HT29 - 5 OYCAR4 - 3 OYCAR4 - 4 OYCAR4 - 5 GYCAR4 - 6 GYCAR4 - 6 SF589 - 3 SF589 - 3 GYCAR5 - 6 OYCAR5 - 6 OYCAR5 - 6 OYCAR5 - 6 HCF/ 6 Hat 9 - 6 HIZB9 - 6 SW480 - 3							TRACTORY TRA	302 239 27 448 309 581 329 45 0 391 408 256 0 648 512 215 711	3771 0 0 1259 0 1208 487 3926 522 0 0 1459 617 2513 3066 444 992 2112	40888 \$2563 \$6030 25013 59035 60522 60476 60609 23961 33862 34224 16007 27907 53162 45568 6783 90711 52580 90711	8615 8637 9240 18176 10000 11477 8801 14924 9741 12881 15917 12742 14894 9772 10469 7292 7377 12210 15796 15796 11567	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	000000000000000000000000000000000000000
http:// http:// http:// http:// http:// http:// OvcAR.4.2  OvcAR.4.3  OvcAR.4.3  OvcAR.4.4  OvcAR.4.5  OvcAR.4.5  SFSW.3  SFSW.3  SFSW.3  SFSW.3  SFSW.3  SFSW.6  OvcAR.4.3  OvcAR.4.3  OvcAR.4.3  OvcAR.4.3  OvcAR.4.3  OvcAR.4.3  OvcAR.4.3  OvcAR.4.4  OvcAR.5.3  OvcAR.6.4  OvcAR.6.5  SW.60.6.5  SW.60.6.5  SW.60.6.5  SW.60.6.5  SW.60.6.5  SW.60.6.5  SW.60.6.5  SW.60.6.4							MALEUM MA	302 239 27 448 309 581 329 45 0 0 0 666 66 66 0 1 1 1 1 1 1 1 1 1 1 1	3771 0 0 0 0 1263 1263 0 1208 4877 2926 522 0 0 0 0 177 2513 3066 444 444 444 445 2112 2112 2112	4988 45030 25954 45030 25954 45030 25954 45030 25954 45030 25954 45030 25954 45030 25955 2	8015 8037 9240 19776 10000 11477 88010 14524 14824 12831 15917 12742 14884 10460 7252 10460 11567 1156	9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	9 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	000000000000000000000000000000000000000
http:// http:// http:// http:// http:// http:// OvcAR4.4  OvcAR4.4  OvcAR4.4  OvcAR4.4  OvcAR4.4  S  SFSB: 3  SFSB: 4  SFSB: 4  SFSB: 4  OvcAR5.3  OvcAR5.3  OvcAR5.3  OvcAR5.4  OvcAR5.6  OvcAR5.6  OvcAR5.6  SFSB: 6  SFS							MACAMINI MAC	302 239 27 448 309 581 329 45 0 0 256 0 0 0 512 225 0 0 0 339 329 329 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	3771 0 0 100 100 1208 0 0 1208 4877 3928 522 0 0 0 9 0 9 1453 2513 2513 2513 2513 2513 2513 2513 25	4888 4888 4893 4893 4893 4893 4893 4893	6915 8937 9249 19176 8001 11477 8001 14924 1728 1728 14934 1722 10460 1727 1727 1727 1727 1727 1727 1727 172	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	000000000000000000000000000000000000000
http://display.com/html://displa							MULEUM MU	302 2399 2494 3494 3597 3297 45 0 0 3911 406.6 648.6 648.6 711 10 10 10 10 10 10 10 10 10 10 10 10 1	3771 0 0 1 0 1 1 0 1 1 0 1 1 0 1 1 0 1 1 0 1 1 0 1 1 0 1 1 0 1 1 0 1 1 0 1 1 0 1 1 1 0 1	4888 4888 4888 4888 4888 4888 4888 488	6915 8937 9240 19176 10000 11477 8601 14224 12881 12742 14854 1477 15917	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	000000000000000000000000000000000000000
http:// http:// http:// http:// http:// http:// OvcAR4.4  OvcAR4.4  OvcAR4.4  OvcAR4.4  OvcAR4.4  S  SFSB: 3  SFSB: 4  SFSB: 4  SFSB: 4  OvcAR5.3  OvcAR5.3  OvcAR5.3  OvcAR5.4  OvcAR5.6  OvcAR5.6  OvcAR5.6  SFSB: 6  SFS							TRUCKENT TRUCKET TRUCK	302 229 27 448.4 309 329 45 45 406 288 0 512 215 711 929 49 49 68 68 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	3771 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	4888 4830 5258 5258 5258 5258 5258 5258 5258 525	6915 6937 9240 19176 10000 10000 14424 15917 12742 14894 14794 1722 17292	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	000000000000000000000000000000000000000	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
http://display.com/stage-1/2014-0-1							MULEUM MU	302 2399 2494 3494 3597 3297 45 0 0 3911 406.6 648.6 648.6 711 10 10 10 10 10 10 10 10 10 10 10 10 1	3771 0 0 1 0 1 1 0 1 1 0 1 1 0 1 1 0 1 1 0 1 1 0 1 1 0 1 1 0 1 1 0 1 1 0 1 1 0 1 1 1 0 1	4888 4888 4888 4888 4888 4888 4888 488	8915 8937 9240 19176 10000 10000 10001 11477 0801 12591 15917 12691 14694 17691 1769	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
http://display.com/html/html/html/html/html/html/html/htm							PRILED TO PRILAD	302 239 27 448, 309 591 1329 45 50 291 45 50 291 140 666 666 666 666 90 90 90 90 90 90 90 90 90 90 90 90 90	3771 0 0 0 0 1298 0 0 1298 497 497 5222 0 0 1498 1498 522 0 0 1498 0 1498 522 0 1498 522	40886 40880	8915 8937 9240 19176 10000 10070 100	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	000000000000000000000000000000000000000	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
http://display.com/stage-1/2014-0-1							PRACEST PRACES	302 239 277 448 309 561 329 455 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	3771 0 0 0 1203 467 3926 522 0 0 0 0 1453 617, 2513 3966 444 444 892 2112 2112 2112 210 20 314 314 314 314 314 314 314 314 314 314	60886 62528 68030 68030 58133 581035 68032 68173 68037	6915 6917 9240 19176 10000 10000 10177 0001 11477 14524 14524 14594 1724 14694 1727 10460 1727 17	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	000000000000000000000000000000000000000
http://display.com/stages/st							PRILED TO PRILAD	302 239 27 448, 309 591 1329 45 50 291 45 50 291 140 666 666 666 666 90 90 90 90 90 90 90 90 90 90 90 90 90	3771 0 0 0 0 1298 0 1298 497 497 522 522 522 522 522 522 522 522 522 52	6888 6839 6839 6839 6839 6839 6839 6839	8915 8927 9240 19176 10000 11477 8801 11427 14224 9741 12981 15917 12210 1698 17917 17918	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	000000000000000000000000000000000000000
http://display.com/stages/st							MPLACENT  PROJECT  PR	302 239 277 277 309 309 455 60 60 60 60 60 60 60 60 60 60 60 60 60	3771 0 0 0 0 1298 487 3926 5522 0 0 1457 457 3936 617 2513 3966 2712 2712 2712 2712 2712 2712 2712 27	60886 60030	6915 6927 9240 19176 10000 11477 6801 11477 14924 14924 17922 14954 17722 10460 17922 1792	9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
http://display.com/stage-1/2014   http							PRACENT PRACEN	3022 2233 277 277 448.8 3299 3291 409.8 3291 409.8 313, 2911 409.8 313, 2151 313, 2151 313, 2251 429.8 40.8 40.8 40.8 40.8 40.8 40.8 40.8 40	3771 0 0 0 0 1203 1203 467 3928 467 3928 617 2513 3066 444 592 2112 2012 2012 2012 2012 2012 2012 20	40486 40300	6915 6927 9240 19776 10000 119776 10000 11477 10477 11477 112742 112742 11527	9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
http://display.com/stage-1/2014   http							INVALINA INVALIDATION OF THE STATE OF THE ST	3022 2339 277 277 4465 3911 3911 45 406 606 607 607 607 607 607 607 607 607 6	3771 0 0 0 1200 0 1200 4677 4677 522 522 522 14559 4444 4559 4647 2513 2566 444 2712 2712 2712 2712 2712 2712 2712	60886 600000 600000 60000 60000 60000 60000 60000 60000 60000 60000 60000 60000 600000 600000 600000 600000 600000 600000 6000000	6915 6917 9240 1077 9240 1077 1077 1077 1077 12742 14594 14596	9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	
http://display.com/html/html/html/html/html/html/html/htm							medium immedium immed	3022 2339 245 345 345 391 391 391 391 391 391 391 391 391 391	3771 0 0 0 1720 1720 1720 1720 1720 1720	69866 6553 66535 66535 66535 66535 66535 66535 66535 66535 66535 66535 66535 66535 66535 66535 66535 66535 67535 6	6015 6017 9020 9020 10176 10000 10176 10000 1026 1026 1026 1026 1026 1026 10	9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	
http://display.com/stages/st							INVALINA INVALIDATION OF THE STATE OF THE ST	3022 2339 277 277 4465 3911 3911 45 406 606 607 607 607 607 607 607 607 607 6	3771 0 0 0 1200 0 1200 4677 4677 522 522 522 14559 4444 4559 4647 2513 2566 444 2712 2712 2712 2712 2712 2712 2712	60886 600000 600000 60000 60000 60000 60000 60000 60000 60000 60000 60000 60000 600000 600000 600000 600000 600000 600000 6000000	6915 6917 9240 1077 9240 1077 9240 1077 1077 1077 1077 1077 1077 1077 10	9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	
http://display.com/stages/st							mediant median	3022 2239 277 277 391 391 45 405 391 405 606 606 606 607 607 607 607 607 607 607	3771 0 0 0 10 0 1263 1263 1263 1263 1263 1263 1263 1263	40486 40500 40500 40500 40500 40500 40500 40550	6915 6937 9920 19776 19786 19786 19786 19896 198	9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	
http://display.com/html://disp							medium immedium immed	3022 2339 277 277 3449 3511 3511 3511 361 361 361 361 361 361 361 361 361 3	3771 0 0 0 1269 1269 1269 1269 1269 1269 1269 1269	### ### ### ### ### ### ### ### ### ##	6915 6917 6920 19176 19176 19177 19171 19171 19171 19171 19171 19177 19171 19177 191	9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0		
http://display.com/stages/st							medium immedium immed	3022 2239 277 277 391 391 45 405 391 405 606 606 606 607 607 607 607 607 607 607	3771 0 0 0 10 0 1263 1263 1263 1263 1263 1263 1263 1263	60886 6050 6050 6050 6050 6050 6050 6050	6915 6917 9926 9926 11977 9926 11977 9927 11477 10401 144724 14984	9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	
http://display.com/html://disp							mediant median	3022 2339 2445 345 345 345 345 345 346 346 347 347 347 347 347 347 347 347 347 347	3771 0 0 0 1288 0 1288 1298 1298 1298 1298 1298 1298 1298	69866 6553 66535 66535 66535 66535 66535 66535 66535 66535 66535 66535 66535 66535 66535 66535 67535 6	6915 8637 9240 19176 9240 19176 19177 19171 19477 19471 19471 19471 19471 19481 1958	9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	
http://display.com/strongs/s							medium immedium immed	3022 2339 277 274 4469 391 45 406 606 607 607 607 607 607 607 6	3771 0 0 0 1269 2299 2299 2392 0 0 0 14159 3075 3075 3075 3075 3075 3075 3075 3075	60486 60502	6915 6917 9240 1077 9240 1077 1077 1077 1077 12742 14994 149	9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0		0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	
http://display.id/html.price							mediant median	3022 2239 277 277 448 458 459 459 459 459 460 660 660 660 660 660 660 660 660 660	3771 0 0 0 0 1263 2269 2269 2269 2522 0 0 0 0 0 1453 2412 2522 2712 2712 2712 2712 2712 2712 27	### (### (### (### (### (### (### (###	6915 8637 9240 19176 9240 19176 19177 19171 19477 19471 19471 19471 19471 19481 1958	9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	
http://display.com/strongs/s							mediant median	3022 2339 244 4469 3511 3511 3511 3511 3611 3	3771 0 0 0 1262 1263 1263 1264 1271 2471 2471 2471 2471 2471 2471 247	### ### ### ### ### ### ### ### ### ##	6915 6917 6920 19176 19176 19177 19171 19471 19471 19471 19471 19471 19471 19471 19471 19471 19471 19489 194	9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	
http://display.com/stages/st							mediant median	3022 2239 277 277 448 458 459 459 459 459 460 660 660 660 660 660 660 660 660 660	3771 0 0 0 0 1263 2269 2269 2269 2522 0 0 0 0 0 1453 2412 2522 2712 2712 2712 2712 2712 2712 27	60886 6050 6050 6050 6050 6050 6050 6050	6915 8697 9240 8697 9240 119770 119770 119770 119771 11977 1	9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	
http://display.id/html   http://display.id/h							mediant median	3022 2339 245 345 345 345 345 345 345 345 345 345 3	3771 0 0 0 1288 0 1288 0 1288 0 1288 0 0 1288 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	69866 6555 6	6915 8637 9726 8637 9726 19730 19730 19730 19731	9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	
http://dispression.com/stages/stage							mediant median	3022 2339 277 4469 591 45 0 391 45 0 0 0 512 2215 10 10 10 10 10 10 10 10 10 10	3771 0 0 0 1269 1269 1299 1299 1299 1299 1299 1299	60000 600000 600000 600000 600000 600000 600000 600000 60000 60000 60000 600000 600000 600000 6000000	6915 6917 9920 19176 19177 19171 191	9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	
http://dispression.com/stages/stage							mediant median	3022 2339 245 345 345 345 345 345 345 345 345 345 3	3771 0 0 0 1288 0 1288 0 1288 0 1288 0 0 1288 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	60000 600000 600000 600000 60000 60000 60000 60000 60000 60000 60000 60000 60000 60000 600000 60000 60000 60000 60000 60000 60000 60000 60000 60000 600000 600000 600000 60000 60000 60000 60000 60000 60000 60000 60000 60000 60000 600000 600000 600000 600000 600000 600000 6000000	6915 8637 9726 8637 9726 19730 19730 19730 19731	9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	

167 Table 3 (contd)

						180	E-4		EFE 47 44	ee o oo ee		1000 No. 11	AFA 14 AP	050 to 00		5EQ 40 MASS	
Tlasue adrenal gland - h	Tulmor-sym	Normal	eym i	Tumor - 10	Tumor celts	norma	ENGOS	P33	46820	1342	187762		11409	2483		599	4349
hmph nade - h		-	_						94539 82024	1004	373187	14301	80824	15392	135195 73538	338	2671
transmery glend - h		<del>                                     </del>	<del>' -</del>						24739	345		11397 1710	51933 2723	6446 266	5276	154	294 306
bran -h			5						54253	1826	188461	6870	929	1184	70030	3190	2311
pancreas - h cerebelum - h	<b></b>		<del>5</del>		<del></del>	├	_	<del></del>	71540 82436			7425 10723	7287 2748	2972 2658	31495 135678	4955 j 6036 i	1246 274
privatery gland - h									87365	232				2404	74670	3059	3472
fatal brain - h			9						103271				3638	1150		7424	8836
procents - h fold introy - h			1			<del></del>	$\vdash$		80242 85084	894 5028			6436 12234	6595 2383	126694 \$5346	1506 5950	4165
proetale, h		1	2						74934	1445	64243	10964	17733	1143	24080	979	86
Setal Inver- h			3			<del></del>			58677 60763			11342 3800	15732	2410		279	2130
eminary gi h fecal lung - h			5						92518				19242	4176		1544	233 3405
akalatal muscis - h			6						57531					505	45674	1077	2017
reagt - h email intentine - h	<del></del>		7	<del></del>					43961 42979			885 3931	4856 14338	2245 2921	31339 21878	632	1632
kidney - h			9						48325			1796		1359	36570	2144	1494
spensi cord - h iow - h			1						54755 40332			21224	5273 2272	1063		787 126	716 413
Splean - h			2						44668	-	129409		30444	4982	17845	0.	622
tung - h			<u> </u>						37827			815	25788	5316		0	452
eterrach -h			5		<del> </del>	$\vdash$		<u> </u>	18016				9695 13224	1998 4542	11933 392139	1806	1333
grymus -h			7						85252	63	422519	10169	38950	8722		1733	317
HPAEC			9			_	28	<b></b>	67087 43670				2437	9015 926		728	755
thyroid gland - h RPTEC			0				. 30		42340				4367	356		- š	
trachee - h		3							78666					3321		602	2353
MAREC Warus - h		3	3		ļ	<del></del>		-	85164 66678				8755	3872 1003		2648	3631
HCAEC			4						\$1717	373		2128	118			242	01
Pancreas - h		ļ			<b></b>			-	46443					0		208	1082
Skeletal muecie - h	<del> </del>	3		<del> </del>	<del></del>				30349					2110 319		208 512	
fetal fiver- h		3	8						56121	649	0	2467	9199	1008	745	947	256
Heart - h	<u> </u>		9					<del></del>	47672 70722					1466		492	<u>ş</u>
thyrnus,h Duodenum - h		+							42191	145		4383	4470	590		2201	3081
Fetat brain - h		-4	2						56960	570	0	6154	4 108	205	1081	3841	386
Selevery of - h	ļ	4	3			<del></del>	—–	<b></b> -	35172 57094	48 129			17131	462	1205	326	
HT218-normal		<u> </u>		<u> </u>		365_			12858			2058	9	97	0 !	356	
H7213-norma			=			363			8245	77		246	222	347	327	584	0
HT157-normal Sev-13	<del></del>	-	_			361	356		16328 82144	1094		248 23735	163 6795	7232	542 5309	1480	- 0
Bay-12						354	354		59687	59	<u> </u>		4027	1119	422	476	- '6
caraballum - h						344			27729		0	239	839	50	D	0	71
RPTEC	ļ	├				342	334		31402 71803		0		96	78 61	479	113	
lymph node - h						332	1		30798	277			52657	253	367	Q!	
h acid SMC 10/21/92 #17						330			47380	237		788	41	. 0	223	54	
Fetal train - h HT398-normal			_		<del> </del>	328 327		<del></del>	70908 50974			29595	10509 10938	93 256	2749 202	1212	
Byrnus,h	<del></del>					326			70826	0			261101	721	750	526	115
HT149 - normal						321			41371		•	0	0	43	166	325	0
HEPM 3d untreded uterus - h		-				320 318			51910 66453			6705 24906		225 9035	3880 4242	1297	166
traches - h		<u> </u>				316			46948	574			129636	7113	2740	893	440
thyroid gland - h						314			44846				64906	5240	1896	. 01	506
extivery gt h prostate, h	<del></del>	-				311	_		61587 47609				39362 25416	1045	347 176	535	- 8
peutury gland - h						307			34764	118	0	1592	19211	875	376	969	157
pencress - h						305			44917 66451				13639	1321 7874	520 407	126 323	596
marremary grand - h breader - h		<del>l                                    </del>	-			302		_	72421			5722		184	4728	1088	
testa - h						298			83198	444		35622	93342	8342	2816	1714	٥
Great - It			_		<u> </u>	297 296			53754 53225	0				1462 6138	3474	1159	91
Splean - h apinal cord - h						294			62962	464			35430	3193	1943	1150	155
email intestine - h						292			41632	39		2123		2505	966	0	155 133
ekeletzi muscle - h bane marrow - h	<del></del>					290 279			60372 50557	27	19		6ZZ31 27722	3687 358	2424	525	896
extremel gland - n						277			84753	27	0	2305	5560	59	0	0	355
HPAEC						275 268	275		37169 38846					0		0	0
HT382-rorms		├				266			44114					. 0		505	605
8ev-11						239 235	239		73567	1154	0	1180	10268	1964	14	Z18 !	144
Bev-6 HT372-normei		$\vdash$				235 234	235	<del></del>	50453 78267	261				557 0	- 0		9
Bey-7		<del></del>				233	233		71554	374				755	0	801	- 8
Bev-6						Z31	231		52712		307	0	1671	1Z27	0	73	196
Bev-1	<del></del>	<del></del>			<del></del>	229 227	229 227	<u> </u>	45448 41869	0				740 942	0,	575	
blackier - N						Z22			33431	505		1299	6262	57	0	56	
Heart - h			=			215			45488 59601					3007	323	139 579	0
retari ingr- h	<del></del>	<del></del>			<del> </del>	214			39067					43	323	131	
placante - h						212_		=	43929		. 0	. 0	11419	2776		397	0
HCAEC	<del></del>	<del></del>				211	Z11	├	34737 70127	290			6938	226		449	43
HMEC						209			48676	155	67	1269	2433	39	1106	0	
Duodenum - h						205		$\vdash$	39299			. 0	7396	35	322	335	120
Shatetal muscle - h Pancreas - h	<b></b>		-			203		$\vdash$	34158		148				565	323	285 D
Institute - h						199			26853				8680			91	Ö
			$\Box$			197			30958		1 8020	566	15657		2026	83	0
HEPM 3d TGFB1 desergent+DNase		<del> </del>	$\dashv$			195			21318 33113				270 65431	58 8113	752	196	3
WI-36 72h						179			21245		0	0	75	_	508	- 0	0
lymph node - h						61			27301				39127	3067	216	53 484	
lung - h		<del> </del>				57			79535 58006	580				7184 769	840 449	126	247
heart - h						55			37503	0	E.9	107	10949	436	0)	01	0
fetal lung - h						53			12635 21581					229 515	749	0:	
fetal liver- h fetal lighter - h		_				49			31744	244	37	341	12404	168		2601	329
HELA-2N-031889					79				38960	536	_0	144	. 0	800	507	419	٥
HELA-4N-031899		$\vdash$			81 83				57302					1365 156	94	714	
HELA-9h-031899 HELA-0h-031899	<del></del>				83				53322 28774	56			- 8		530	-/14	- 8
HELA-61-031899					68				55350	0	0	3037	904	291	299	195	Ô
HELA-81-021209					8				55168 52933	- 0				1197 2796	365	1429	9
HELA-101-031899 HELA-111-031899			-		92				52933 42462					2796 992	426	Q I	
HELA-12h-031899					96				34825	98	0	0	299	1009	0	313	0
NCI-H322M		=			146				15500			0		3313 1753	285 401	605 I	160 282
NCI-HI50 NCI-H522					150				20164					701	. 401	163	357 57
SNB-19					152		=		18076	0	211	261	395	3491	846	0	57
SNB-75			-		154 156				27275 18225					4401 892	114	6938	175 D
SF-268 SF-296			+		158				9339	114	0		110	369	241	743	141
CCRF-CEM			$\Box$		160				16835					Z54		29	779
	. 7		I		162				14305					923		0	779
DU-145 HCT 116			- 1		164	, ,			13034		351	570	422	542	1 0:	576	D1

168 Table 3 (contd)

			-			-			1							
Cont.1	Tumor-sym	Normal-sym	Tutmor - 10	Tumor cells	Normal	Endos	1633	8EQ 17 A	A SEC 20 5	11 22 P	T#6EQ 25 A	N SEQ_29_04	550 31 08		SEQ 40 M 4 SE	EQ 044
786-0				168		T	Τ.	4325	3 141	5 104	4 248	2263	8374	109	01	
Xan-J	<del> </del>	+	<del> </del>	169	+	+	+	5270 3004		01 462				1109	0 0	12
CRL 1441 RNA 8/30				181				1195		0 48	8 1871	242	339	32	197	
781T unregated • DName KB poly A•		<del>                                     </del>	<del> </del>	183		_	+	2131 2356		0	0 0			691	120	
HOS poly A+		Ţ		196			-	3910 2361	41	0!	0 1156	3112	1682	145	46	120
UACC-82			<u> </u>	200	_	<del> </del>	1	1919		0 187	4 1696 9 1264			750	371 559	120
MCF-7/ADR-RES			<del></del>	202	+	$\vdash$	1	1260	1 31	4	714	405	215	178	0	43
UTOS (Mundy) poly an WISH (Collegen) poly An	<del>                                     </del>	<del></del>	<del> </del>	204 206	<del>†                                      </del>	+	+	1299	)	0 0	1294	572	149	- 0		
458 medulio mRNA		<u> </u>		208		$\overline{}$	$\vdash$	8354		0 104	1 3506		411	. 0	411	
CCL137 RNA 3/21/88 WI-38 72h 0.5%FBS, 24h 10% FBS	<del></del>	+	<del> </del>	218 219	<del>!</del>	<del> </del>	+-	2119 2806		0 56	3 8			149		134
CRL 1441 - TPA (24h) 8/30				220	-		1	1472	5	0 133	31 0		355	862	0	
Ka-1 Ka-2	<del> </del>	<del>1</del>		223			1	28116 3254	5	4 2				157	361	
Ken-4				225				3753	3 4	3 804	154	0	721	0	6871	
HOP-92 MOLT-4	<del> </del>	+	<del> </del>	241	+	+	+-	1870		0 1338	59			636	0	50
EXX				243			-	2245	38	7 303	1936	537	2757	371	01	
HL-60 NCI-HZ3	+	<del></del>	<del></del>	244 245	+	+-	+-	33141 2904;	2 399	0 90				2603	1154	1434
RPMI 6226				746				34429	5)	0] (	309	567	1614	134	222	60
AS49/ATCC SR	<del> </del>	<del>                                     </del>	<del> </del>	247 248	<del></del> -	+	+	38516 19586		01 (351				153		401
CVCAR-3				249				2744	3	200	669	652	1417	284	3625	260
OVCAR-4	<del> </del>	<del> </del> -	<del></del>	250 251	+	+	+-	1033		0 5278 8 1077	7: 613		2395 587	1074	<u>208</u>	
UQ-31				252	1 -		1 ===	13456	1	01 415	s	242	757		0.	116
OVCAR-5 SN12C	<del></del>	<del> </del>	<del> </del>	253 254	+	+	<del> </del>	50297 39550	11	9 3366	1757		7068 483	535	1034	<del>27</del> 7
OVCAR-6		ļ		255			T	16467	15	9! 573	582	512	215	819	104	0
IGROV1	<del></del>	<del>                                     </del>	<del> </del>	256 257	+	+	+	45485 36125		0 16504 1, 290	740		1340	190	279: 231:	699
SK-MEL-2				258	I	1		34735	73	71 299	1017	0	536	377	73.	208
SK-OV-3 SK-MEL-5	<del></del>	<del> </del>	<del> </del>	259 260	+	<del></del>	<del> </del>	17172	26. 21	2: C		312	339	0	157	128
SF-539		<u> </u>		261				38531	65	5 1771	924	955	3468			408
SK-MEL-28 K-562	<del> </del>	<del> </del>	<del> </del>	262	1	<del> </del>	+	34495		0 337	617	1130	2525	598	262	336
UACC-257				264			=	25143	16	4 0	606	210	617	97	612	336
M14 MCF7	<del>                                     </del>	<del></del>	<del></del>	265	t	<del>                                     </del>	+	10129 68939	4	0 2893		176	1109	279 2556	4481	583
MDA-M8-43S				269				26815	iL (	0 678	815	40	503	5	6'	
MDA-N	+	<del></del>	<b>——</b>	270	<del>                                     </del>		+	38490	72	0 0	550	7537	0 492	416 2143	1472	276
Y79 poly A+				273				102505	97	z   2309	0	922	6961	534	1356	625
HTB36 24h TPA RNA 6/23	<del> </del>	<del> </del>	<del> </del>	300	<del> </del>	<del>-</del>	<del>                                     </del>	38003 47107		0 0	9054	8253	4347	3093	387	0
HELA-EXP-031899				313		$\blacksquare$		19309		00	0	Q	31	299,	42	<u>-</u>
HTB36 Oh RNA			<del> </del>	322	<del>                                     </del>		┼	52969		787	7168 265		2751	1124	503	0
458 medulo RNA				324				58268		0	18772	5011	0	840	363	0
NCI-H226 HOP-62	+	<del></del>		336	<del> </del>	<del> </del>	<del>                                     </del>	23074		164		1027	334 2365	1532	1281 231	593
MDA-MB-231				338			<b>—</b>	35092		P643	45452	11567	18823	5581	1838	1619
U251 PT cells poly A+	<del> </del> -	<del> </del>	<del></del>	339	<del> </del>	├	—	33958	<del>  ,</del>	19509		7782	63609 1453	10227	1071	5160 46
23				341				23466	130	283	3466	925	913	386	01	262
HCC-2996 SW 4020	<del> </del>	<del></del>	<del></del>	343		-	<del> </del>	17769	- 5			774 500	355 203	673 451	1336	423 649
HT192				346				42880	97	0	2671	17366	2232	1485	. 0	73
COLO 205 HT218				347	+	<del>                                     </del>		12549 26025	├──			9440	109	01	757	- 0
K94-12				349			=	21716		1595		7779	350	0;	531	349
HT151 A496				350 351		<del></del>	<u> </u>	55696 23633	698			8252	152	406 903	511 826	279
H7393 RXF 190				352 353				63325	483				2060	. 0	0	0
TK-10				355	l	-		23449 42915	208	55.15		337 8242	2050 6629	212	425	578
Matria-3M He 578T				357 359	$\vdash$			74434	551	91082	18863	11096	31229	6343	1293	2753
HT213			50	339				23715 41730			1805	12170	1418	425	372	0
HT258			52 54				-	34514 37801				39548	259	6.	0	0
HT155			56				<u> </u>	37790				12374	20	1041	55 591	143
HT163 HT170	F		3.8				_	38017		9		4844	Oi	406	141	0
HT172			62					59964 31376		1 0	871		67	607'	638	357
MT138			63 64				_	41851		245		17086	01	171	0:	0
HT178 HT154			65			$\sqsubseteq$		37107 32270					781	665	443.	193
HT 180			56 67					26571		. 0	901	3611	683	731	2343	27
HT189			68					20113 27825	267	0	1324	1192	2544 350	725	1630 704	
HT143 HT190			69 70					20413 19364	135	475		6121	0	01	558	257
HT145			71					27515	675	0	7647	23622	0	0.	231	248
HT227 HT302			72 73					30606 37705	0	0	2489		423	0	\$371	. 31
HT314			74					36927	475	1 0	131	18869	3131	0	200	9
HTT317 Mediafoblescoma #425 11/8			76		<del></del>		$\vdash$	66238 30458	916	_ 0		6,2568	2603	0: 266	429	0
HT323			78					51648	187	538	0	12817	182	9.	0:	90
HT327 HT335			80 82				==	43116 47965	159	0			97	163 i 330 :	849: 160	
HT146			85					13508	209	. 0		2507	0:	183	36	40 90
HT348			170		$\vdash$			51446 37227	631 266		162 454	16397	69	126	725	99 114
HT311			185					38852	0	. 0		5668 6527	1906	550	780	
HT311								19305 35781	0				194	9	307 1356	78
HT311 HT398 HT140			187													
HT311 HT390 HT140 HT281 HT372			187 189 191					43132	0		30	1744	4271	0,	319.	305
MT311 MT398 MT140 MT281 MT372 TCGP			187 189 191 207					43132 36117	•	159	1		9 i	01	0.	53
HT311 HT130 HT140 HT221 HT321 HT372 TCGP HT150			187 189 191 207 216 217					43132 36117 18433 17447	205 84	159	1 1107 352	1329		01 01		53 0 142
HT311 HT389 HT140 HT281 HT372 TG0P HT307 HT307			187 189 191 207 216 217 224					43132 36117 18433 17447 39703	205 84	159 293 0	1107 352 8188	1329 1273 19489	0 0 153 17	01 01 02 799	0 344 : 0	53 0 142 61
H7311 H7389 H7140 H7261 H7327 TGGP H7160 H7307 H7307 H7308			187 189 191 207 216 217 224 226 228					43132 36117 18433 17447 29703 33028 40577	0 205 84 0 0	159 293 0 0	1 1107 352 8188 215	0 1329 1273	0 0 153	01 01	0: 344 : 0	53 0 142 61
HT311 HT388 HT140 HT140 HT281 HT322 TCGP HT180 HT367 HT367 HT367 HT367 HT377			187 189 191 207 216 217 224 226 228 230					43132 36117 18433 17447 39703 33028 40577 45559	0 205 84 0 0 6 428	159 293 0 0 0 1 1	1 1107 352 8188 215 0	0 1329 1273 19489 10361 9937 12382	0 0 153 17 0 250	01 02 799 03 03	0 344: 0 0; 0; 253: 334:	53 0 142 61 0 287
HT311 HT391 HT398 HT140 HT140 HT281 HT327 TGGP HT150 HT307 HT307 HT307 HT307 HT371 HT377 HT371			187 189 191 207 216 217 224 225 228 230 236 281					43132 36117 18433 17447 33703 33028 40577 45559 44406 10088	0 205 84 0 0 6 428 0	159 293 0 0 0 1 1 187 0	1 1107 352 8188 215 0 0 1940	0 1329 1273 19489 10351 9937	0 0 353 17 0 250	01 0: 0: 799 0: 3	0 344 0 0 0 253	53 0 142 61 0 287
HT311 HT381 HT381 HT140 HT120 HT121 HT322 TG6P HT160 HT372 HT378 HT377 HT377 HT377 HT377 HT377 HT377 HT377 HT377			187 189 191 207 216 217 224 225 226 230 236 281					43132 36117 18433 17447 39703 33028 40577 45559 44408 10086 58656	0 205 84 0 0 6 428 0 368 903	159 293 0 0 0 1 137 0 0	1 1107 352 8186 215 0 0 1940 0	0 1329 1273 19489 10351 9937 12382 8161 63 25039	0 0 1833 17 0 250 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 344 0 0 0 0 253 334 4271 0	53 0 142 61 0 287 0
HT311 HT381 HT381 HT140 HT120 HT121 HT327 HT327 HT303 HT377 HT307 HT377 HT377 HT377 HT377 HT377 HT378 HT378			187 189 191 207 216 217 224 226 226 228 230 236 281 299 301					43132 36117 18433 17447 39703 30028 40577 45559 44406 10086 58656 43347 17927	0 205 84 0 0 6 428 9 358 903 335 233	159 283 0 0 0 1 187 0 0 0	1 1107 352 8188 215 0 0 1940 0 3690 3594 895	0 1329 1273 19489 10351 9937 12382 8161 63	0 0 153 17 0 259 0	0 0: 0: 799 0: 3: 0: 127	9: 344: 0: 0: 0: 253: 334: 427:	53 0 142 61 0 287 0 0
HT311 HT388 HT140 HT140 HT140 HT121 HT22 HT22 HT22 HT327 HT327 HT327 HT327 HT327 HT327 HT327 HT327 HT327 HT327 HT327 HT327 HT327 HT327 HT327 HT327 HT327 HT327			187 1889 191 207 216 217 224 226 228 230 236 281 299 301 315 317					43132 38117 19433 17447 33703 3028 40577 45559 44406 10086 58656 48347 17827 30990	0 205 84 0 0 6 428 9 368 903 3355 253	159 293 0 0 0 0 1 1 187 3 0 0 0 0 0 0 1 1 187	1 1107 352 8188 215 0 0 1940 0 3690 3564 895	0 1329 1273 19489 10361 9307 12382 8161 63 25039 15153 1607 40456	0 0 253 17 0 256 0 0 0 0 0 145	01 01 02 799 03 3 0 0 227 0 0 473 303 704	0; 344; 0; 0; 0; 253; 334; 427; 0; 0; 221; 0;	53 0 142 61 0 287 0
HT311 HT388 HT140 HT140 HT140 HT121 HT227 HT227 HT327 HT318			187 189 191 207 216 217 226 226 220 236 281 299 301 317 319 325					43132 28117 19433 17447 28703 30020 40577 45559 44406 10086 56656 48347 17927 30990 37896 29856	0 205 84 0 0 6 428 0 368 903 335 253 449 0	159 293 0 0 0 1 187 0 0 0 0 115 0 0	1 1107 352 8188 215 0 1940 0 3690 3564 896 2263	0 1329 1273 19469 10351 9337 12382 8161 63 25039 15153	0 0 353 17 0 256 0 0 0 0 0	01 02 799 03 03 01 327 0 0 473 383	9: 344: 0: 0: 0: 253: 334: 427: 0: 0: 221: 0: 714: 379:	53 0 142 61 0 287 0 0
HT311 HT391 HT398 HT140 HT120 HT120 HT322 TG6P HT160 HT307 HT303 HT307 HT307 HT307 HT307 HT308 HT308 HT308 HT308 HT308 HT308 HT308 HT308 HT308 HT308 HT308 HT308			187 189 191 207 216 217 224 225 226 229 236 281 299 201 315 317 319 325					43132 26117 19433 17447 29703 33028 40577 45559 44406 10086 56656 46347 17927 37896 23656 24967	0 205 84 0 0 428 903 335 253 449 0 0	159 283 0 0 0 1 187 0 0 0 0 115 0 152 0 152	1 1107 3522 6188: 2155 0 0 1940 0 3690 3564 696 2263 5232 175 2286	0 1329 1273 19489 10361 12382 81611 631 25039 15153 25039 1637 40459 1822 0 17868	0 0 0 1533 17 0 256 0 0 0 0 0 145 0 0 965	01 02 799 03 31 00 327 0 0 473 393 393 704 154 130	0; 344; 0 0 0 0 253; 334, 427; 0; 0; 0; 221; 01, 714; 379; 149; 149; 151;	53 0 142 0 0 287 0 0 0 0 0 0 0 0 0 0 0
MT311 HT388 HT140 HT140 HT140 HT140 HT140 HT160 HT367 HT367 HT367 HT370 HT370 HT370 HT370 HT370 HT370 HT370 HT370 HT370 HT371 HT381 HT381 HT381 HT381 HT381	163		187 189 191 207 216 217 226 226 228 230 236 281 299 301 317 319					43132 36117 19433 17447 39703 33029 46577 45559 44406 19086 19086 4947 17927 30990 37896 25856 4997 57210 22111	0 205 84 0 0 6 428 0 368 903 335 253 449 0 0 959	159 283 0 0 0 1 1 187 0 0 0 0 0 115 0 522 0 0 2 34135	1 1107 352 6188 215 0 0 0 1940 3690 3690 3564 2263 2283 1775 2288 12307 2256	0 1329 1273 19489 10361 9937 12362 8161 53 25039 15153 1637 1037 17868 18792 433	0 0 0 353 17 0 259 0 0 0 0 145 0 965 208 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	01 02 7991 02 33 0 0 473 0 0 473 383 704 154 156 233 233 7551	0; 344: 0 0; 0; 0; 0; 253: 334: 427; 0; 0; 0; 221; 0; 149; 149; 149; 0; 0; 776;	53 0 142 161 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
HT311 HT381 HT188 HT140 HT121 HT121 HT122 HT22 HT372 HT372 HT377 HT378 HT381 HT381 HT381 HT381 HT381 HT381 HT381 HT381 HT381 HT381 HT381 HT381 HT381	161		187 189 191 207 216 217 224 225 226 229 236 281 299 201 315 317 319 325					43132 36117 18433 17447 33703 33029 40527 45559 44400 10086 59656 48347 17927 305900 37896 23856 23856 23967 57210 221111 22304	0 2055 844 0 0 0 6 428 90368 903 335 253 449 0 0 0 0 544	159 293 0 0 0 1 1 187 0 0 0 0 0 0 115 52 0 0 2 2 2 3 1 3 3 7 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	1 1107 352 8188 215 0 0 0 1940 0 3554 5956 2283 533 175 2288 2530 2530	0 1329 1273 19489 10361 9937 12382 8161 63 25039 15152 1637 40458 1822 0 17869 18792 413	0 0 0 353 17 0 259 0 0 0 0 145 0 0 965 208 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	01 01 799 01 31 0 0 327 0 0 473 363 704 130 486 233 7591 15184	0: 344: 0: 0: 0: 0: 253: 334: 427: 0: 0: 221: 0: 379: 149: 215: 0: 758: 99: 99:	53 0 0 207 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
MT311 HT388 HT140 HT140 HT140 HT140 HT140 HT160 HT367 HT367 HT367 HT370 HT370 HT370 HT370 HT370 HT370 HT370 HT370 HT370 HT371 HT381 HT381 HT381 HT381 HT381	765 161 159 159		187 189 191 207 216 217 224 225 226 229 236 281 299 201 315 317 319 325					43132 36117 19433 17447 39703 33029 46577 45559 44406 19086 19086 4947 17927 30990 37896 25856 4997 57210 22111	0 205 84 0 0 6 428 0 368 903 335 253 449 0 0 959	159 2813 0 0 0 1 187 0 0 0 0 0 0 0 0 0 15 0 0 0 15 15 0 15 218095 218095 1155 21805549	1 1107 352 6188 215 0 0 0 1940 0 0 3594 595 2283 2288 2288 2288 2288 2288 2288 228	0 1329 1273 19489 10361 9937 12362 8161 53 25039 15153 1637 1037 17868 18792 433	0 0 0 353 17 0 259 0 0 0 0 145 0 965 208 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	01 02 7991 02 33 0 0 473 0 0 473 383 704 154 156 233 233 7551	0; 344: 0 0; 0; 0; 0; 253: 334: 427; 0; 0; 0; 221; 0; 149; 149; 149; 0; 0; 776;	53 0 142 161 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0

169 Table 3 (contd)

Tiesue	Turnor-sym	Normal-sym	Tumor - to	Tumor calls	Normal	Endos	p53			SEQ 47 A			SEQ 51 KL			
DaPang:7								85383	570	729	1	2  9	10			)! 0
DaPeng-8		ļ						26499 44303	716	374 156			0	<del> </del>		9
DaPeng-9 DaPeng-11					-			24987	1					<del> </del>	1	0
DaPeng-12								95743		495	il' c					0
DaPeng-10			<u> </u>			-		20110 7684	284 964	211	1					
DaPeng-1 DaPeng-2				<b></b>				3139		38	1		il			6
DaPang-3								698	1703	265					1	0
OsPang-4	ļ ——	<u> </u>						26952 40680	324	51					3	
DaPeng-5 DaPeng-6								32900	20			0 _ (		1	)	0
A549 - 8							w	1956		90	1	9	0		2	
EKVX · 8							mutant	959		0	<del> </del>					0
HCT-116 - 7 HCT-116 - 8	<del> </del>				<del> </del>		wi .	771	122	55		0 0	0	- 0		0
HT29 - 1							mutant	310		144		01	1 0			! 0
HT29 - 7	<u> </u>	ļ			<del></del>		mutant	- 0	<del> </del>	25	1	0 0	3			): 0
HT29 - 8 SF539 - 7	H						wi	1397	937	36	·	0 0	2			0
SF539 - 8							3	3330			Ţ					
SF-268-7	<b></b>						mutant	1 <u>7076</u> 15222			;		0 0		0 0	
SF-268-8 OVCAR-4 - 7						-	w	1233	25	0		01 (	; 0	,	) (	
OVCAR-4 - 8							¥	12764		175			2			
OVCAR-5 - 7 OVCAR-5 - 8							muteni muteni	4732 3132		0						. 0
MCF-7 - 8							w	3375	440	) 0	1	9 (	0 0		21 0	0
ADR-RES - 8							mutant	538		0	ļ!	9	9			
HeLs - 8 SW480 - 7	<del> </del>		<del></del>	·	├	-	HPV E6	1097	717	22			0	<del>                                     </del>		0
SW480 - 8							mutani	412	1	72						0
H1299 - 8					-	<u> </u>	mutani		163	10	1	0 0	0 0		12	!
C33A - 7 C33A - 8	<del></del>	<b></b>		<del></del>	<del> </del>	<del>                                     </del>	mutani	444		-	<del>                                     </del>	0 0	0 0	1 - 2		
U2OS - 7							mutant	28619	148	84	H	0) (	) 0			0
U2OS - 8					<u> </u>		mutant	4758	418		<del> </del>		0 0			0
He68 - 7 He68 - 8	<b> </b>			-		<del> </del>	w	1393 512	324	1 0	<del>                                     </del>	0 0		<del>                                     </del>		0
							wi	1504	41	1 0	)!	0 0	0		1 .	0
WI 38 - 8 456 medulo RNA CRL1572 3/17/89	$\vdash$					<del></del>		340			13-	5793	2685	399	596	5988
9a-4	<del></del>	<del> </del>		<del>                                     </del>	<u> </u>	84		642		0	185	5574		84		12425
HT368										0	50	1 467	3 0		1	1 16708
HT378				<b> </b>	-	├	-	10732		34		0 441		81		
HT385	<del> </del>	<del></del>		<u> </u>		=					1	614	168		1	24562
Ber-3						173		53	9							
Bev-5						175		0		58						
h karatnocytes 2/25/92 #10	<del> </del>					177				93				112		196
Bev-10						237		0		19		3 406				
HTB10 h fibroblesia 3/31/92 #12					<del> </del>	<del></del>		- 0				0 753: 3 4548				
prostate. h	<del> </del>											1 2983				5650
MINING-OS poly A+								915		0						
SA-OS (Alundy) poly A+ MK poly A+			<b></b>	<del></del>	<del> </del>			9		57	5	5 114L		257		
HCT-116 - 3							w	396	Z	2 3		0 0	) 0	1		0
HCT-115 - 4							w	438 127								
HCT-116 - 5	1			1			wi									- 4
HACT-118 - 6						)	wi	1178				0	0		H C	)
HCT-116 - 6 A549 - 6							¥ ¥			0		0 0	0			. 0
A549 - 6 HT29 - 3							wi muteni	16959		0 0		0 0	0 0			0
A549 - 6 HT29 - 3 EKVX - 6							w			0 4 0 247		0 0	0 0		0	0
A549 - 6 HT28 - 3 EKVX - 6 HT29 - 4 HT29 - 5							wi mutani mutani mutani	0 16959 561 0 1078		0 0 4 0 247 0 0 0 7 28		D C	0 0	0	9	0 0
A549-6 HT25-3 EKVX-6 HT29-4 HT29-5 HT29-6							wi muteni muteni muteni muteni muteni	0 18959 561 0 1078		0 0 4 247 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0		0 0 0 0 0 0	0 0 0	0 0		0 0
ASIG-6 HT29-3 EKVX-6 HT29-4 HT29-5 HT29-6 OVCAR4-3							wi mutani mutani mutani	0 16959 561 0 1078	100	0 4 247 0 28 1 244 1 52 3 30		0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0			0 0
A549 - 6 HT29 - 3 EKX - 5 HT29 - 4 HT29 - 5 OVCAR4 - 3 OVCAR4 - 4 OVCAR4 - 5							wi mutani mutani mutani mutani mutani wi wi	0 18959 561 0 1978 9 5253 0	100	0 0 4 1 247 0 0 28 244 0 52 3 30 0 0 0 0 0			0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0			0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
A549 - 6 HT29 - 3 EKVx - 6 HT29 - 4 HT29 - 5 HT29 - 5 OVCAR4 - 3 OVCAR4 - 4 OVCAR4 - 6							wri crusterni crusterni crusterni crusterni crusterni crusterni wri wri wri	0 16959 561 0 1078 0 \$253 0 2869	100	0 0 0 4 244 244 3 30 30 30 32 32 33 32 33 32 33 32 33 32 33 33 33						0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
A549 - 6 HT29 - 3 ECVC - 5 HT29 - 4 HT29 - 5 HT29 - 5 OVCAR4 - 3 OVCAR4 - 5 OVCAR4 - 5 OVCAR4 - 5							wi mutani mutani mutani mutani mutani wi wi	0 18959 561 0 1978 9 5253 0	100 100 100 100 100 100 100 100 100 100	0 4 247 20 28 20 244 52 30 0 0 0 32 140 32			0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0			0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
A540-6 HT25-2 EKYX-6 HT29-4 HT29-5 OVCAR4-4 OVCAR4-5 OVCAR4-5 OVCAR4-5 OVCAR4-5 SF330-3 SF330-4 SF330-4							wri emutani emutani emutani emutani emutani wri wri wri wri wri	0 19959 561 1078 0 9 5253 0 2969 0 4462 3256 591	100	0 4 247 247 28 28 29 29 29 29 29 29 29 29 29 29 29 29 29		0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0				0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
ASS0.6 HT25.2 EXV.7.6 EXV.7.6 HT25.5 HT20.6 CVCAR4.4 CVCAR4.5 CVCAR4.5 CVCAR4.5 CVCAR4.5 CVCAR4.5 CVCAR4.5 CVCAR4.5 CVCAR4.5 CVCAR4.5 CVCAR4.5 CVCAR4.6 SPESS.6 SPESS.6							wi mutani mutani mutani mutani mutani wi wi wi wi wi	0 16959 561 1078 9 5253 0 2869 4462 3256 591	100 100 100 100 100 100 100 100 100 100	0 0 4 1 247 247 247 247 247 247 247 247 247 247		0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0				0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
A540-6 HT28-2 EKIX-6 HT28-4 HT28-6 HT28-5 OVCAR-1-3 OVCAR-1-5 OVCAR-1-5 OVCAR-1-5 OVCAR-1-5 SF330-3 SF330-6 OVCAR-1-5 OVCAR-1-5 OVCAR-1-5 OVCAR-1-5 OVCAR-1-5 OVCAR-1-5 OVCAR-1-5 OVCAR-1-5 OVCAR-1-5 OVCAR-1-5 OVCAR-1-5 OVCAR-1-5 OVCAR-1-5							ori counterni counterni counterni counterni counterni coni coni coni coni coni coni coni co	0 19958 561 0 0 9 5253 0 2969 0 4462 3256 591 1280	100 100 100 100 100 100 100 100 100 100	0 0 4 247 0 247 1 248 1 244 1 32 1 30 1 32 1 40 2 1 18						0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
A540-6 HT32-3 EKVX-6 HT32-4 HT32-6 HT32-5 OVCAR4-3 OVCAR4-3 OVCAR4-6 OVCAR4-6 SF530-3 SF530-6 OVCAR5-1 OVCAR5-1 OVCAR5-1 OVCAR5-1							ensiterati ensiterati ensiterati ensiterati ensiterati ensiterati ensiterati enti enti enti enti enti enti enti en	0 1995a 561 0 1978 0 2553 0 0 2869 0 4462 3256 599 1280 2366	277 277 277 26 26 31	9 9 9 4 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9						
ASSO. 6 HT73: .3 EXVx. 6 HT3: .1 HT3: .1 HT3: .1 OVCARA - 1 OVCARA - 3 OVCARA - 5 OVCARA - 5 OVCARA - 5 OVCARA - 6 SFSSS: .3 SFSSS: .3 SFSSS: .3 SFSSS: .6 OVCARA - 5 OVCARA - 5							eristeri erusteri erusteri erusteri erusteri eri eri eri eri eri eri eri eri eri	0 0 0 1 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0	100 100 100 100 100 100 100 100 100 100	30 9 9 4 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9						
ASSO. 6 HT73: .3 EXVX. 6 HT73: .1 HT73: .1 EXX							eristeri eristeri eristeri eristeri eristeri set set set set set set set set set set	0 1995s 5616 0 0 5253 0 2968 2268 2255 2368 2268 2375 2376 244 244 244 244 244 244 244 244 244 24	101 101 101 101 101 101 101 101 101 101	0 9 9 9 4 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9		D				
ASS0-6 HT73-1-3 EKVX-6 EKVX-6 EKVX-6 EKVX-6 HT73-5 HT73-6 CVCAR8-4 CVCAR8-4 CVCAR8-5 CVCAR8-5 CVCAR8-6 GVCAR8-6 EK46-6 HK46-6							enstant enstant enstant enstant enstant enstant enstant enstant ent ent ent ent ent ent ent ent ent e	0 10058 100558 100550 10058 100550 1005	11 100 100 100 100 100 100 100 100 100	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0		0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0				
ASSO. 6 HT73: .3 EXVX. 6 HT73: .1 HT73: .1 EXX							enterni enterni enterni enterni enterni enterni enterni ent ent ent ent ent ent ent ent ent ent	0 10055 561 10055	100 (100 (100 (100 (100 (100 (100 (100	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0		0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0			
ASSO-6 HT73-1-3 EKVX-6 HT39-4 HT39-4 HT39-5 HT39-5 OVCAR4-3 OVCAR4-3 OVCAR4-5 OVCAR4-5 OVCAR4-5 OVCAR4-5 OVCAR4-5 OVCAR4-5 OVCAR4-5 OVCAR4-6 SFSSS-3 SFSSS-3 SFSSS-6 OVCAR5-3 OVCAR5-3 OVCAR5-3 OVCAR5-3 OVCAR5-3 SFSSS-6 OVCAR5-3 OVCAR5-3 SFSSS-6 SFSSSS-6 SFSSSSS-6 SFSSSSS-6 SFSSSSS-6 SFSSSSS-6 SFSSSSS-6 SFSSSSS-6 SFSSSSSSS-6 SFSSSSS-6 SFSSSSSS-6 SFSSSSSS-6 SFSSSSSSSSSSS-6 SFSSSSSSSSSS-6 SFSSSSSSSSSSSSSSSSS-6 SFSSSSSSSSSSSSSSSSSSSSSSSSSSSSS							eristeri eristeri eristeri eristeri eristeri set eristeri set eri eri eri eri eri eri eri eri eri eri	0 0 1005	6 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0		0				
A549.6 HT725.2 EKVA.6 E							eriutari eriutari eriutari eriutari eriutari eriutari eriutari eri eri eri eri eri eri eri eri eri e	0 10958	100 110 110 110 110 110 110 110 110 110	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0			0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0			
ASSO. 6 HT73: -3 EXV. 6 HT73: -1 HT73:							oriustani ersustani ersust	0 0 10955	6 44 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0		0				
A549-6 HT25-2 EKVA-5 EKVA-6 EK							oriustani resultani	0 0 10955	100 100 100 100 100 100 100 100 100 100	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0						
ASSO 6 HT73: .3 EXV. 6 HT73: .1 HT73: .							oriustani ersustani ersust	0 0 10955	6 44 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0		D				
A540-6 HT73-1-3 EKYX-6 HT73-1-4 HT73-1-4 HT73-1-4 HT73-1-4 HT73-1-5 UVCAR4-3 UVCAR4-3 UVCAR4-3 UVCAR4-5 UVCAR4-5 UVCAR4-5 UVCAR4-5 UVCAR4-5 UVCAR4-6 SFS33-3 SFS33-6 OVCAR5-6 UVCAR5-6 UVCAR5-6 UVCAR5-6 UVCAR5-6 UVCAR5-1-6 HT73-6 HT73-6 HT73-6 HT73-6 UVCAR5-1-6 UVCA							with control of contro	0 109556	6 44 64 64 64 64 64 64 64 64 64 64 64 64	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0		S				
A540-6 HT25-2 EXVA-6 EXVA-6 EXVA-6 EXVA-6 EXVA-6 EXVA-6 EXVA-6 EXVA-6 EXVA-6 EXVA-6 EXVA-6 EXVA-6 EXVA-6 EXVA-6 EXVA-6 EXVA-6 EXVA-6 EXVA-6 EXVA-7 EXVA-7 EXVA-7 EXVA-7 EXVA-7 EXVA-7 EXVA-7 EXVA-7 EXVA-7 EXVA-7 EXVA-7 EX							with a constant const	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	( ) ( ) ( ) ( ) ( ) ( ) ( ) ( ) ( ) ( )	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0						
A540-6 HT73-1-3 EKYX-6 HT73-1-4 HT73-1-4 HT73-1-4 HT73-1-4 HT73-1-4 HT73-1-5 UVCAR-1-3 UVCAR-1-3 UVCAR-1-5 UVCAR-1-5 UVCAR-1-5 UVCAR-1-5 UVCAR-1-5 UVCAR-1-5 UVCAR-1-5 UVCAR-1-6 HT73-1-6 HT73-1-6 HT73-1-6 HT73-1-6 HT73-1-6 HT73-1-7 SW450-1							well moutant moutant moutant moutant moutant moutant moutant moutant moutant well well well well well well well wel	0 10955	6 1 27 1 1 1 1 1 2 1 1 1 1 1 1 1 1 1 1 1	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0		8				
ASSO 6 HT73-13 EXVX-6 EXVX-6 EXVX-6 EXVX-6 HT73-6 CVCARR-13 CVCARR-3 CVCARR							well moutant moutant moutant moutant moutant moutant moutant moutant moutant well well well well moutant moutant moutant well moutant well moutant mou	0 1995	6 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0		S				
A540-6 HT73-1-3 EXVX-6 HT73-1-5 EXVX-6 HT73-1-5 UVCAR-1-4 UVCAR-1-3 UVCAR-1-5 UVCAR-1-5 UVCAR-1-5 UVCAR-1-5 UVCAR-1-5 UVCAR-1-5 UVCAR-1-5 UVCAR-1-5 UVCAR-1-5 UVCAR-1-5 UVCAR-1-6 HT39-6 UVCAR-5-1 UVCAR-6-1 UVCAR							well moutant moutant moutant moutant moutant moutant moutant well well well well well well well wel	0 0 10955	6 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0		S				
A549.6 HT73-2 EKVA-6 EK							well moutant moutant moutant moutant moutant moutant moutant moutant moutant well well well well well well well moutant moutan	0 0 1995	6 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0						
A540-6 HT725-2 EXVA-6 EXVA-6 EXVA-6 EXVA-6 EXVA-6 EXVA-6 EXVA-6 EXVA-6 EXVA-6 EXVA-6 EXVA-6 EXVA-6 EXVA-6 EXVA-6 EXVA-6 EXVA-6 EXVA-6 EXVA-6 EXVA-7 EXVA-7 EXVA-7 EXVA-7 EXVA-7 EXXA-7 E							wei mendent mendent mendent mendent mendent wei en det en	0 19955   561   19955	6 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0		8				
A540-6 HT73-1-3 EXVX-6 HT73-1-1 HT73-1 HT73-1-1 HT73-1							wer menden't revolunt. Trouten't revolunt with the second	0 0 1995	6 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0						
A540-6 HT725-2 EXVA-6 EX							wei mendent mendent mendent mendent mendent wei en det en	0 19955   561   19955	C   C   C   C   C   C   C   C   C   C	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0		0				
A540-6 HT72-13 EXV.A-6 EXV.A-6 EXV.A-6 EXV.A-6 EXV.A-6 EXV.A-6 EXV.A-6 EXV.A-6 EXV.A-6 EXV.A-6 EXV.A-6 EXV.A-6 EXV.A-6 EXV.A-6 EXV.A-6 EXV.A-6 EXV.A-6 EXV.A-6 EXV.A-7 EXV.A-7 EXV.A-7 EXV.A-7 EXV.A-7 EXV.A-7 EXV.A-7 EXX.A-7							wer menden't revolunt. Trouten't revolunt with the second	0 1995 561 1	6 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0						
A549-6 HT725-2 EKVA-6 E							wer menden't revolunt. Trouten't revolunt wer menden wer menden wer menden wer menden wer menden werden wer	0 0 1995	C   C   C   C   C   C   C   C   C   C	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0		S				
A540-6 HT73-1-3 EXV.2-6 HT73-1-1 HT73-1 HT73-1-1 HT73-1 HT7							wei mendeni me	0 19956 561 1995	6 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0		S				
A540-6 HT73-1-3 EXVX-6 HT73-1-1 HT73-1-1 HT73-1-1 HT73-1-1 HT73-1-1 HT73-1-1 HT73-1-3 HT73-1-3 HT73-1-3 HT73-1-3 HT73-1-3 HT73-1-3 HT73-1-3 HT73-1-3 HT73-1-3 HT73-1-3 HT73-1-3 HT73-1-3 HT73-1 HT73-1-3 HT73-1 HT73-1-3 HT73-1 HT73-1-3 HT73-1 HT73							wer menden't revolunt. Trouten't revolunt wer menden wer menden wer menden wer menden wer menden werden wer	0 0 1995	6 (1) (1) (1) (1) (1) (1) (1) (1) (1) (1)	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0						
A540-6 HT25-2 EXVA-6 EXVA-7 EXVA-7 EXVA-7 EXVA-7 EXVA-7 EXVA-7 EXVA-7 EXVA-7 EXVA-7 EXXA-7 EX							wei mendeni me	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	6 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	0						
A540-6 HT73-1-3 EXVX-6 HT73-1-1 HT73-1-1 HT73-1-1 HT73-1-1 HT73-1-1 HT73-1-1 HT73-1-3 HT73-1-3 HT73-1-3 HT73-1-3 HT73-1-3 HT73-1-3 HT73-1-3 HT73-1-3 HT73-1-3 HT73-1-3 HT73-1-3 HT73-1-3 HT73-1 HT73-1-3 HT73-1 HT73-1-3 HT73-1 HT73-1-3 HT73-1 HT73							wei mendeni me	0 0 1995	6 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0						
A549-6 HT73-2 EKVA-6 EKVA-7 EK							wei mendeni me	0 0 1995	6 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0		S				
A540-6 HT726-2 EXVZ-6 EXVZ-7 EXVZ-7 EXVZ-7 EXVZ-7 EXVZ-7 EXVZ-7 EX							wei mendeni me	0 0 1995	6 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0						
A549-6 HT73-2 EKVA-6 EKVA-7 EK							wei mendeni me	0 0 1995	6 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0						
ASSO 6 HT725 - 2 EXVX - 2 EXVX - 5 EXVX - 6 EXVX - 6 EXVX - 6 EXVX - 6 EXVX - 6 EXVX - 6 EXVX - 6 EXVX - 6 EXVX - 7 EXVX - 7 EXXX  7 EXXX  7 EXXX  7 EXXX  7 EXXX - 7							wei mendeni me	0 0 1995	6 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0		8				

170 Table 3 (contd)

Tipeve	Tumor-sym	Normal-ey	n Tumor - to	Turnor cells	Normal	Endos	io33	ISPO M A	4 SEC	4 850 60 4	ALCEO ET LIE	1000 (C.C.	SEO 68 HIS	-r		
scrend gland - h		1			1				45399	1372	4 10216	11737	167361	4759	24187	161827
lymph node - h bone marrow - h	+	1 3		+	<del> </del>	+	┿	186						7405	31327	144050
mannery gland - h		1						102	8369		9 24326			3999	<u>86136!</u>	30783
percress - h	<del> </del>	1 5	<del></del>			$\vdash$	_	1567	33741		7 6670	113657	27844	36791	135121	88774
corebath.m - h	i i	7		<del>                                     </del>	<del> </del>	+	<del> </del> -	2734	39449					7267	39350	88925
proutery gland - h	$\vdash$					$\blacksquare$		2771	66397	1496				5844	23795	150166 126706
fetal brain - h	+	10	<del></del>	<del> </del>		+	┼	7654						5280	23245	130701
fetal ludrey - h		11						3098						4685	294581 38782	118927 202584
prostore, h	<del> </del>	12		<del> </del>	-		-	2873	23467	1503		8510	18409	4446	8670	180598
eatwary of h		14			<u> </u>	<b>t</b>	<u>†</u>	1962	20668					2114 2253	47817 23301	95705
fatel lung - h sheletel muscle - h	<u> </u>	15				Τ		4579	50513	939	9 6440	27133	27710	3092	32855	175336
Peart - h	<del> </del>	17			<del>                                     </del>	+	├─	3544 1236	34574					1781	9575	126486
small intestine - h	<u> </u>	18		<b></b>				2013	18551	1729				18761	15805	108323 254953
todney - h spensi cord - h	<del> </del>	19		<del> </del>	<del> </del>		<del> </del>	1838 2970				7388		2068	17635	150364
two - h		21						4795					29454 39372	1989 2313	7081 10324	130873
Splean - h lung - h	<del>                                     </del>	22		+			-	1065			9 2932	3727	20754	2087	4681	114231
etomach -h	1.	24				<del> </del>		1619				4273 4031	20688	2193 2181	6428 6584	1,25866 357434
terte - h	Ļ	75						5462	103115	523	10154	6356	10159	4776	20107	122829
trymus -h	<del> </del> -	27	+	<del>                                     </del>	├	20	├-	1676				17350 4196	19356	4763	33850	115427
thyroid gland - h		29				Τ		2594	29474	246		11290	12372 11291	3412 3114	13897	93109 90705
RPTEC traches - h		30		<del> </del>	<b>├</b> ──	30	_	508 5137	12784		1729	1851	15158	3649	13265	96954
HMEC		32		<u> </u>		<del> </del>	_	18853	21362			24729		3380 2697	21166 9425	714306 78553
HCAEC		33		<u> </u>	-			1208	41525		6685	34917	19410	2493	15360	68824
Parcreas - h		35		<del> </del>			<del>-</del>	554				435 290	17803 5241	1992	4218	72012
symph nade - h		36						1745	12072	5592	2849	638	7798	2332 3831	5669 3205	128381 77707
Statetal muscle - h_ fatal liver - h	<del></del>	37	+	<del> </del>	<u> </u>	<del> </del>		621			1071	2029	4538	905	2524	38353
Heart - h		19						896	6677				14398 4578	2211 885	508741 1733	76358 58107
thymus,h Duodenum - ft	<u> </u>	40				-		1510	11513	1144	4500	53	5096	2118	84821	94284
Fetal tran - h		43				<u> </u>	<u> </u>	927				405 551	9086	1544 3645	9281	55243
Sarvary of n		43						1366	4890		2394	0.	42751	1451:	3676,	124700 81426
teste - h HT218-romal		4	<del>-                                    </del>	-	365	<del>                                     </del>	<del></del>	1650				130	13181	2101	10939	125863
HT213-normal					363			0	8044				743	1102	501	20873 24903
HT157-name Ber-13		<del> </del>		<del> </del>	381 356	356	H	451 299	2420				171	1861	335	30436
Bev-12					354	354		1760	128945	9	21	5137 3012	10567 6067	7821	14920 2525	172795 95002
constatum - h	<b> </b>				. 344		=	. 0	4508	72	83	228	428	2304	1611	30731
RPTEC	<del>                                     </del>		<del></del>		342	334	-	1246		715 19083		357	701	2360 4284	443	32872
hymph node - h h what SMC 10/21/92 #17					337			153	12413		1318	7	1559	3969	274	165421 65390
Fault brain - h	<del>                                     </del>		<del></del>	<del></del>	330 328	1		256		537		94	24	2990	0	43499
HT398-resmal					327			1215	4596	- 30		1683	12093	1962	3750 ·	95415 36102
Promatin					326	$\vdash$		+63	76773			5123	48.23	8646	1169	99548
HEPM 3d untrested					320		_	1317		57		214	1316	2550 4217	2089	- 37663 56214
trianue - h					318			0	65419	1050	1252	1531	15960	11203	30226	123975
traches - h throad aland - h	<del></del>				316			0	40355 42997	905	1959	2194	12222	8263 6871	140783	104686
selvary gi h					311			. 0	8659			- 137	2738	2519	96901 4532	101244
prostore, h privitory gland - h					309			858	5480 14108	- 0	233	129	1622	2462	3058	70453
percrees - h					305			000	6503	0	114	735 0	1127 2636	2496	2133 3386	39646 55383
marrowary gland - h					303			104	26315	589	467	220	6627	4345	16318	98789
blackler - h tuste - h		<del></del>	_		302 298	<del>  </del>		1973	19158	7296		1502	9250 19319	4496 7297	7821 · 29073 <sub>1</sub>	65038 140418
iver - h					297			2987	40917	2131	330	t896	8744	6235	13181	101946
Spheem - h epinel cord - h			+		296 294			666	9515	1484	137	117	2690	3770	5859	51130
email intestine - h					292			205	48295 7475	316		1208	1941	7977 2923	11556 9383	112019 64902
plunistal muscle - h					290			2187	53059	1405	547	843	11136	6446	29427	164567
bone marrow - h schwai gland - h	<u> </u>		+		279				765	1572 56	375	01	405	1603 2156	1886	30233 24322
MPAEC					275	275		182	3675	56	0		504	2487	01	39020
HT392-normal HT382-norma			+		268 266			2212	3036	729		2671	0	3137	407	52419
Ben-11					239	239		623	8248	- 0		163	1078 7268	3510 4208	2147 16995	71286 157428
Box 6					Z35	235		9	3824		0	0	2750	2873	1723	61030
HT372-remid Ber-7			<del></del>		233	233		3431	3130	412		227	1502	3430 2666	503 4367	80667 60074
Bev-6	-				Z31	231		778	4003	٥	57	0	1455	2754	3914	31581
Ber-2 Ber-1	<del></del>		+		Z29 Z21	229 227		197	5734 3974	. 0		196	1062	2969	2380 5947	48128 40717
backfor - h					222		_=	250	4008	- 0	17	196	1520	2495 2660	363	44379
Heart - h	-		+		215	<del>- 1</del>		0	1810 48161	0		28	5243	3097	1770	107397
fetal four- h					213			0	2869			328	3148 456	336S	5934 i	81804 41566
PROMINE - N MCAEC			+	$\overline{}$	212	211		138	3720	0		153	3470	2961	7793	55692
letal brain - h					210		_	135	21571 68541	0		250	979	3260	4176	45376 62140
HMEC Ducaterum - h			+		209	==		779	3094	q	4	199	01	2108	- 01	37896
Shalatal musicle - it					205			319	3296	43		29	483	16S2 2208	236 124	40649
Pancrese - h					201			9	3155	_363	95	0	189	2439	364	43068
Salvary gi - h			+ $ -$		199	-		385	9731 5746	- 0 865	159	338	2122	2245	390	44576
HEPM 3d TOFB1 detergent+ONate					195			584	3763	0	0	32	538	1518	Z052	35673
WI-38 72h			+		193			0	29305	348		25	254	1356	2652	47888
hymph reade - h			1		179 61			- 0	3118 4438	0	204		2063	1363	8791	22161 35753
lung - n					59			0	(6888)	803	158	88	3840	3001	\$597	125182
todney - h heart - h			<del> </del>		57 55	<del></del>		1173	3419 7101	0	567	0 822	2379	2158	3645 1888	56857 47950
fetal king - h					53			273	3213	0	0	0	1020	2135 777	6221	35486
fetal fiver- h fetal techney - h	—∓		+		49	=		390	3097 3589	0	158	176	905	1157	6005 5247	35043 65106
HELA-25-031899				79				5981	7753	- 8	67	519	1798	2195 2759	21226	73028
HELA-IN-031899 HELA-9N-031899	-		+	B1		=		5076	2561	. 0	196	0	791	2339	8863	73685
HELA-0h-031899			+	83				1983	2784	654	162	203	1276 2720	1297	62121 40701	75474 33775
HELA-61-031699			T	88				94	12562	253	. 01	61	01	1643:	4396	70122
HELA-03-031899 HELA-101-031899	<del></del> -		<del>                                     </del>	90	-	$-\Box$		2321	3276 6586	- 0	165	82	565	17441	3048	61476
HELA-11h-031899	=		1	92				1224 476	936	- 0	193	192	1344	1761	7822: 3546	88409 44168
HELA-12h-031899 NCI-H022M			$\vdash$	96		$\rightarrow$		328	587		91	0	931	14091	1928	78433
NCI-HISD			+	146	<del></del> +	-+		706	5027	0	3263 703	283	907 432	4168: 31941	47496 13322	26944 29260
NCI-H52Z				150		二		01	3419	0.	225	99	378	1671	2959	24405
SNB-19 SNB-75	<del></del> F		<b></b>	152				258	3161 T	- 01	373 753		1514	2329	17171	24596
SF-268			<del></del>	156		+		460	3779	432	753 i	40	1122	3295 1851	8489	16046
SF-295	-			158		=		0	Q)	0	57	436	732	555	20431	12390
CCRF-CEM DU-145			+	160	<del></del>			365	1895 2190	0	144	196	921 ( 1288 )	1957	13460	15083 18145
MCT 116				164				10	4548		248	01	471	13741	10125:	18145
											_					

Table 3 (contd)

Section   Sect	Tinsue	Yumanan	Morral	Tuesa In	17	This	E-4	1-02	Teno 42 A	Alera w e	dece	riaco so s	1000 -2 51				
Color	Hs 578T	155	NOT ME SYM	Tumor - 16	Tumor cells	Normal	Cnoos	P33									
Color	MCF-7/ADR-RES	153	ļ			I					0 7041	1 721	187	. 0	15559	0	859
Column	M14	149							6330	37	1 2222	15029	2725	257	4104	075	
Second	UACC-257	145	<del> </del>	+	<del> </del>	<b>├</b> ──	├						111		32383		
March   10	SK-MEL-28	144				ļ			2695	7	1 1024	140	2016	634	4087		
			+		<del> </del>	├	<del></del>	<del>-</del>									
Column									3099	29	7 692	3 202		65	1287	0	329
Column	HCT-15	139						<u> </u>	5473	44	5 2528	2765	1572	495 287			189 D
Column			+	ļ					45060	146	6 86468	4322	243	254			
19	LOX IMVI	136							25010	1	0 161759	1512	680				
Second   1985			+		<del> </del>	<del> </del>	<del> </del>	<del>                                     </del>	4320	43	7 29571 A 15976						168
Company				T	_				37409	34	5 18771	1178	0	458	3812	721	68
Sept. 138   19   19   19   19   19   19   19   1	HCC-2998	131															
Column							-		3606	32	9 91730	1353	617				
Margin   M	RXF 393	128							4044	30:	5 8266	3148	2477	2041	26924		- 0
Second			<del> </del>	<del>                                     </del>			-	<del> </del>				5153					
Margin   19		125	<b> </b>			Ε			3785	) 1	0 50238	7597	1172	551	26608	156	0
Section   100	RPMI 8226	123		$\vdash$					50455	73	7 8134	2600	2182			423	01
Main			+	<del> </del>		⊢			32576								
March   10									28309	78.	2 17195	881	532	1023	4039	0	D
Color	K-562	118			<u> </u>				54213	58	2 18145	2128	337				
Section   11	CCRF-CEM			+	<del></del>			<b>—</b>	42598	1500	106942	5320	2239	2583	9251	1228	1110
100   100	OVCAR-3	115	1	F					52017	541	8 47691	1242	959	303	10348	2443'	0
1.528	HOP-62		<del></del>	<u> </u>	<u> </u>		<u></u>	<u> </u>	34665 19576		6 14022	2825	. 0			0	
Line	SF-295		-	ļ					40830	25	7 17908	700	708	1154	5386	417	637
Color	SF-268	110							30245	6	4 55487	972	185	303			572 568
Section	NCI-H522 U251		1						44511		61026	565	813	276	8039	01	94
SEASTEDN   19	NCI-H460	107							28896	356	5 75179	436	405	603	17568	808	152
Manual Property of the Company of	NCI-H322M	105										3058	455	369		884 746	
Section   192			+	-							2 13625	1417	451	2644	32654	156	625
March   Marc	SK-OV-3	102							33170		18596	3841	522	200	18891	343	59 51
Second Second	IGROV1		<del> </del>			-							140	203	29599	0	491
Color	EKVX	99							25017		14573	1622	. 0	642	34177	0	0
Name	HOP-92	97										1074	366	197	12792	492	
Name   1996   1997	h fibrobiaeta 3/31/92 #12 h est# SMC 10/21/92 #17	48											5270	341	401	200	184
Add	h karasnocytes 2/25/92 #10	46							29126	. 66	23461	1117		92	10270	344	
Main	AS4B - 1	- 78		<del> </del>				w .						4388	5277	1704	111
MAS - 1	A549 - J							*	0		9	531	124	4578	539	1033	0
Section   Sect	A549 - 5								0		0					890	
MAY	A549 - 7 EKVX - 1	<del></del>		-								1340				22.70	0
March	EKVX - 4								0		0	2098	4210	10881	330	190	
WE   0   0   0   130   150	EKVX - 5								0		0	284				705	
West   Color   BKVX - 7 MCF-7 - 1	<del></del>	<del> </del> -			$\longrightarrow$			0								- 0	
MCF-7-1   William   Color	MCF-7 - 3							*	0		0	16	1048	2997	0	492	0
MCC-1-1	MCF-7 - 5																
MASA-12									- 0	0	0						D
MARKES	ADR-RES - 3							multer!	0	0	0	1148	3462	4039	1056	. 81	0
ADMARES	ADR-RES - 5							mutani	- 0								
WI 30 - 2	ADR-RES - 7	<del></del>						TRUCKEN!	0		0					498	0
MISS 1	W1 36 + 3							wt .	0	. 0	0	665				0	0
MISS   1	WI 38 - 5	-	<del></del>		<del></del>				- 8								
HIPV   E	WI 36 - 7					$\Box$		w .				1458	3377	5828	312	0.	
Mary   Mary	Ptet_a - 3							HPV E6	. 0	0	0	842	849	4257	546	0	. 0
Higher	Hala-4 Hala-5	<del>                                     </del>			<del></del>	-		HPV E6		<del>                                     </del>	0	250					
Higher	Halp-7	F						HPV E6	0	0	0	1543	274	4769	0,	0:	
Miles	H1299 - 3							muteril	0	0	0	. 0	431	2212			
Miles	H1299 - 4 H1299 - 5	<del> </del>		<del> </del>	<del></del>	<del></del>		mutani mutani					123	4674	421		
HECHT   1	H1299 - 7							COLUMN 1	- 0	0	0	458	1853	1167	101	0	ő
Miles   Mile	EKVX - 2							TELESTE .			0	1435	520	20773	QÎ		01
No.   No.	HCT-116 - 1 HCT-115 - 2			<del></del> -	<del></del>	——₹			0	- 0	0						
PS-93-7	HT29 - 2							muturn!	0	0	0	10141	25411	1846	496	0)	
SF-280-1	SF539 - 2							*		0	0	819	5447	744	750		
DVCARR4 - 1	SF-268-1 SF-268-2					=		muteri		0	0	2143	3277	4430	635	0	
DVCARS - 1	OVCAR-4 - 1							M		0	0	1444	2283	19120	251	652	O.
PACARS - 2	OVCAR-5 - 1					=			0	- 0		1743		13774			
DBA-RES - 2	OVCAR-5 - 2 MCF-7 - 2	-						THE PARTY		0		1268	3797	1735	535	0	- 0
MM-0   MM-0	ADR-RES - 2							THE STATE OF	. 0	0	0	776	1963	945	0	44	0
Websit	SW480 - 1			Ŧ	T	-1			0		0	941 478	1918	8717			
	SW480 · 2									0		1209	703	2907	0	4498	0
13334 2   1840 2	C33A - 1							nuturi.	0				4354				
	C33A - 2			-		$\neg$		mustant		0	0	604	1162	690	200	373	0
wide 1.1         wif.         0         0         0         1 4327         4551         6728         0         609         0           wide 1.2         wide 1.2         wide 1.2         0         0         0         1 1863         29355         2631         0         0         0         1 1863         29355         2631         0         0         0         1 1863         29355         2631         0         0         0         2 1864         0         0         0         0         1 1863         2 1864         0         0         0         0         0         0         2 1864         0 <td>U2OS - 2</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td>nuteri  </td> <td></td> <td>0</td> <td>. 0</td> <td>6100</td> <td>11204</td> <td>3320</td> <td>1903</td> <td>3626</td> <td>. 0</td>	U2OS - 2							nuteri		0	. 0	6100	11204	3320	1903	3626	. 0
W130-2	He68 - 2																
debut - 2         0         0         0         4465         20d t         0         405         0         0         0           debut - 2         0         0         0         5420         11649         13409         0         1371         0           debut - 4         0         0         0         0         5450         41855         4028         0         1037         0           debut - 5         0         0         0         0         0         4850         2861         0         282         0         0           debut - 5         0         0         0         0         1705         340         316         143         0         0	W1 38 - 2					_			0		0	2505	6897	5771	442	19	0
	Michael - 2			$\longrightarrow$					0		0						
	Methal - 3					=		$\neg$	0	0	0	5420	11049	13409	0	1371	0
46hai - 6 0 0 0 1706 340 315 143 0 0	Michai - 5								0		0	4520	2581	. 0[	282		0
80g-2 0 0 40 21721 273 603 01 0	Matchael - 6 Matchael - 8	<del></del>			<del></del>	-				0	- 0						0
	Michael - 9							=	Ö		9		21722				

172 Table 3 (contd)

G	17	Te			72 .	14 .	7	1222 12								
DaPang-Z	Fumor-sym	Norma)-sym	Tumor - 1a	Tumor cella	Normal	Endos	p53	SEQ 17 A	A SEQ 20 S	G 5EQ 22 P	TISEO 26 A	SEQ 25 DE	SEQ 31 D	05EQ 032 A	USEQ 40 MA	SEQ 044 1
DaPeng-8				+		_	+				21694	8478	31596	2728		
O=Peng-9				1					6		912	8543 1598	25973			
DaPang:11	Ţ		T						0		7501	9216				
DaParo-12	+	<del></del>	<del> </del>			+			0 (	0 0	3497	3288				
DaParg-10 DaParg-1	+		<del></del>	+	+	+	+		0 - 0	9	6482	298				
DaPero-2			1	<del>                                     </del>	+	<del>                                     </del>	+									
DsPeng-3										<u> </u>	4784					
Osffeng-4	<del></del>			-		1-		1		0	1944					
DaPang-5	+	+	-	<del> </del>	+	<del> </del>							327		2183	
A549 - 8	<del></del>	<del> </del>	+	<del> </del>	+	+	1	<del> </del>		0 0						
EKVX - 0					+	1 -	materi	1		<del> </del>			9852			
HCT-116 - 7						<u> </u>	w						3043		619	
HCT-116 - 8	+		<del></del>	<del></del>		-	₩					6117		761	01	
HT29 - 7	+	<del> </del>	+	<del> </del>		<del> </del>	meters		91	9 9				631		
HT29 - 8		1		1	+	<del> </del>	muteri							- 0		
SF539 - 7			T.			1	im.						2178 2843	1075		
SF539 - 8		T					wt		1	1 0			7922	562	200	
SF-268-7 SF-268-8	+	+	<del> </del>	<del></del>	<del></del>	<del>↓</del> -	mutent						2732	1198	1054	
OVCAR-4 - 7	<del> </del>	<del> </del>	<del> </del>	<del></del>	+	-	STREETS						4622	394	0	
OVCAR-4 - 6			Ī										13609	0 685	3736	
OVCAR-5 - 7	ļ.,						metent		)				21830	- 0	37.50	0
OVCAR-5 - 8 MCF-7 - 8			<del> </del>	<del> </del>	+		mutent		) 0			2853	7100	2593		. 0
ADR-RES - 0	+	+		+	+		mutent				ļ <u>0</u>		1521	1 0	190	. 0
HeLa - 8	1			<del>                                     </del>	1	<del>                                     </del>	HEV EG						3321	1418		
SW480 - 7						L	mutant		0				4765 4942	1418		<del></del> š
SW460 - 8	<del> </del>	<b></b>	-				mutant			. 0	0	870	4326		1168:	
H1299 - 8 C33A - 7	+	<del></del>	<del> </del>	<del>                                     </del>	+	<del>                                     </del>	mutant					4781	2495	298	491	
C33A - 8	<del>                                     </del>	1	<del></del>	<del></del>	+	<del> </del>	mutani	<del>- </del>					2718	1002	837	0
U2OS - 7							mutant	<del></del>		: 0			3016	865 977	1215	
U2OS - 6	<del> </del>						muteri		. 0	. 0	31	4880	8016	0	0:	
Hu68 - 7 Hu68 - 8		<del></del>	<del>                                     </del>		+	-	wt		. 0	0		345	3165	144		0
W138 - 8	<del></del>	1	-	<del> </del>	+	<del>                                     </del>	1.1					1183	3374	1882	D:	
458 meduto RNA						İ	<u> </u>	37688				299	3574 1447	6182	455	
CRL1572 3/17/89		1						25584	578	736		4685	27	\$79	15	<u>0</u>
HT368	<del></del>	+	-			84		59510		0	1007	3021	1552	0	136	
HT378	<del>1</del>	+	+	<del> </del>	+	<del> </del>	-	32554		0		21100	3573	79	0	301
HT385		1		<del>!</del>	+	<del></del>	$\vdash$	37556 76812		386		2860	1359	316		0
HT308								21762	851	- 0			1103	185	873	574
Be-3	<del></del>	<del> </del>			-	173		38821	35	1 0			1010	76	178	0
Ber-S Ber-9	<del></del>	<del> </del>		<del></del>	<del> </del>	175		19950		0			- 60		171	10
h terretmocytes 2/25/92 #10	-	<del>                                     </del>	<del> </del>	<del> </del>	<del></del>	<del>'''-</del> -	<del> </del>	39076 \$0327	0	142			643	0		110
Bev-10						237		45162	257			733	2244	400		
HTB10	<del></del>										1379	3593		0	ol o	
h fibroblanta 3/31/92 #12 prostate, h	<del></del>	<del>├─</del> ─		<del> </del>	╄	├		44374	88			4810	70	0	261	0
MNNG-OS pary A+	1	<del>                                     </del>	<del></del>	<del> </del>	<del> </del>			29035 24878	236	1075	3562	5762 3701	1721	1048		<del></del>
SA-QS (Mundy) poly A+																
	ļ										10786			01		
MK paly A+								27097 32124	0	261	10786 12609	5681	674	1962	963	483
MK paly A+ HCT-116 - 3							**	27097 32124 0	0	261	10788 12609	5681 10417 1768	674 478 4464	1962 297		483
MK pay A+ HCT-116 - 3 HCT-116 - 4							*	27097 32124 0	0 0	261 0	10788 12609 11	5681 10417 1768 3318	674 478 4464 7970	1962 297 113	963 24 0	483 0
MK poly A+ HCT-116 - 3 HCT-116 - 4 HCT-116 - 5 HCT-116 - 5								27097 32124 0	0	261 0	10788 12609 11 0 1789	5681 10417 1768 3318 1899	674 478 4464 7970 3247	1962 297 113	983 24 0	483 0
MK poly A+ HCT-116 - 3 HCT-116 - 4 HCT-116 - 5 HCT-116 - 6 A549 - 6							1 1 1 5	27097 32124 0 0 0 0	0 0	0 261 0 0	10788 12609 11 0 1789 598	5681 10417 1768 3318 1899 2679	674 478 4464 7970	1962 297 113	963 24 0	483 0
MK poly A+ HCT-115 - 3 HCT-116 - 4 HCT-116 - 6 HCT-116 - 6 HCT-116 - 6 HCT-20 - 3							eri eri eri musterei	27097 32124 0 0 0 0 0	0 0 0	0 261 0 0 0	10768 12609 11 0 1789 598 0	5681 10417 1768 3318 1899 2679 2201 4624	674 478 4464 7070 3247 7618 52 7875	1962 297 113 0 267 0 1143	983 24 0 0 245	483 0
MK poly A+ HCT-116 - 3 HCT-116 - 4 HCT-116 - 4 HCT-116 - 5 HCT-116 - 6 HCT-19 - 6 HCT-19 - 6 HCT-19 - 6 HCT-19 - 3							ud ud ud mutani mutani	27097 32124 0 0 0 0 0 0	0 0 0 0 0 0	261 0 0 0 0	10786 12609 11 0 1789 598 0 148	5681 10417 1768 3318 1899 2679 2201 4624 1949	674 478 4464 7070 3247 7618 52 7875 2376	1962 297 113 0 267 0 1143	963 24 0 0 245 302 513 435	483 0
MK pay A- MCT-118 - 3 MCT-118 - 4 MCT-118 - 5 MCT-118 - 5 MCT-118 - 5 MCT-118 - 6 MT29 - 3 EVXX - 6 MT29 - 4 MT29 - 4 MT29 - 5							eri eri eri musterei	27097 32124 0 0 0 0 0	0 0 0 0 0 0 0	0 261 0 0 0 0	10786 12609 11 0 1789 598 0 148 0	5681 10417 1768 3318 1899 2579 2201 4624 1949 323	674 478 4464 7970 3247 7618 52 7875 2376 3234	1962 297 113 0 267 0 1143 0	983 24 0 0 245 302 513 435	483 0
MK pay A+ MCT-116 - 3 MCT-116 - 4 MCT-116 - 5 MCT-116 - 6 MCT-116 - 6 MCT-126 - 6 MCT-126 - 6 MCT-126 - 6 MCT-126 - 6 MCT-126 - 6 MCT-126 - 6 MCT-126 - 6 MCT-126 - 6 MCT-126 - 6 MCT-126 - 6 MCT-126 - 6 MCT-126 - 6							unt unt unt muclamit muclamit muclamit muclamit muclamit muclamit	27097 32124 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0	10788 12609 11 0 1789 598 0 148 0 1239 1070	5681 10417 1768 3318 1899 2679 2201 4624 1949	674 478 4464 7970 3247 7618 52 7875 2376 3234 3867 5679	1962 297 113 6 267 9 1143 0 181	963 24 0 0 245 302 513 435	483 0
MK pop A+ MCT-118-3 MCT-118-4 MCT-118-5 MCT-118-6 MCT-118-6 MCT-118-5 MCT-118-5 MCT-118-5 MCT-118-5 MCT-118-5 MCT-118-6 MCT-18-5 MCT-18-6							ort ort ort ort ort ort ort ort ort ort	27097 32124 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	000000000000000000000000000000000000000	0 281 0 0 0 0 0 0 0 0 0 0 0	10786 12609 11 0 1789 598 0 148 0 1239 1070 0 1203	5681 (0417 1768 3318 1899 2679 2201 4624 1949 322 3886 2090 1613	674 478 4464 7970 3247 7618 52 7875 2376 3234 3867 11856	1962 297 113 0 267 0 1143 0	963 24 0 0 245 302 513 435 0 363 0	483 0
MK pps A+ MCT-116 - 3 MCT-116 - 3 MCT-116 - 4 MCT-116 - 5 MCT-116 - 5 MCT-116 - 6 MCT-10							unt unt unt unt marisoni maris	27097 32124 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0	0 281 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	10786 12609 11789 1789 598 0 1446 0 1239 1070 0	5681 (0417 1768 3318 1899 2679 2201 4624 1949 323 3886 2090 1613 708	674 478 4464 7970 3247 7618 52 7875 2378 3234 3867 5879 11856 8721	1962 297 113 0 0 257 0 1143 0 0 181 0 800	963 24 0 0 0 245 302 513 435 0 363 0 1055 689	483 0
MK pps A+ MCT-116 - 3 MCT-116 - 3 MCT-116 - 4 MCT-116 - 5 MCT-116 - 5 MCT-116 - 6 MCT-1 6 MCT-							ort ort ort ort ort ort ort ort ort ort	27097 32124 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 281 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	10786 12609 12789 11 0 1789 9 0 148 0 1239 1970 1203 0 1203	5681 (0417 1768 3318 1899 2679 2201 4624 1949 323 3886 2090 1613 708 3034	674 478 4464 7970 3247 7618 52 7875 2276 3234 3667 11856 6721 13755	1962 297 113 0 357 0 1143 0 1811 0 800 870 0	963 24 0 0 245 302 513 435 0 363 0 1055 589 3849	483 0 0 0 0 0 0 0 0 0 0 0 0 0
MK pps A+ MCT-116-3 MCT-116-3 MCT-116-4 MCT-116-4 MCT-116-5 AG-1-6 MT29-3 BVX6 MT29-3 BVX6 MT29-5 MT29-5 MT29-6 MT29-							unt unt unt unt marianni maria	27097 32124 9 9 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 281 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	10786 12609 111 0 1789 9 0 148 0 1239 1070 0 1239 0 1203 0 959 813	5681 (0417 1768 3318 1893 2679 2201 4624 1949 323 3886 2090 1613 708 30679	674 478 4464 7970 3247 7618 52 7875 2376 3234 3867 5873 11856 8721 13755 2575	1962 297 113 0 257 0 1143 0 181 0 800 0 1759 0	903 24 0 0 0 245 302 513 435 0 0 363 6 689 3849	483 0
MK pop A+ MCT-118 - 3 MCT-118 - 4 MCT-118 - 4 MCT-118 - 5 MCT-118 - 6 MCT-118 - 6 MCT-12 - 3 EVX-1 - 6 MCT-1 - 6  OVCAR-4 - 3 OVCAR-4 - 6 SFS30 - 1 SFS30 - 3							unt unt unt unt unt unt unt murtaret murtaret murtaret murtaret murtaret unt unt unt unt unt unt unt unt unt un	27097 32124 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 2761 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	10786 12609 111 0 1789 598 0 148 0 1239 1070 0 1203 0 959 913	5681 10417 1768 3318 1899 2679 2201 4624 1949 323 3886 2090 1613 708 1613 708 4103 1647 4103	674 478 4464 7970 3247 7616 52 2376 3234 3667 5679 11856 6721 13758 2575 1572	1962 297 113 0 0 267 0 1143 0 181 0 0 800 870 0 275 271 155	963 24 0 0 0 302 445 9 132 435 0 0 365 1055 689 3849 284 746	483 0 0 0 0 0 0 0 0 0 0 0 0 0
MK pps A+ MCT-116-3 MCT-116-3 MCT-116-4 MCT-116-4 MCT-116-5 AG-1-6 MT29-3 BVX6 MT29-3 BVX6 MT29-5 MT29-5 MT29-6 MT29-							unt unt unt unt unt unt mutannt mutannt mutannt mutannt mutannt mutannt mutannt mutannt unt unt unt unt unt unt unt unt unt	27097 32124 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 2851 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	10788 12609 117 12609 117 12609 117 127 1270 1270 1270 1270 1270 1270 1	5681 10417 1768 3318 1899 2679 2201 4624 1949 323 2090 1613 708 3034 10679 4103 1863 1292	674 478 4464 7970 3247 7618 52, 2376 3234 3667 5679 11856 6721 13755 2575 1672 2380	1962 297 1133 0 0 1143 0 181 0 0 800 870 0 1759 211 155 0	963 24 0 0 0 246 302 513 435 9 1055 689 3849 284 746 109	483 0 0 0 0 0 0 0 0 0 0 0 0 0
MK pps A+ MKT-116-3 MKT-116-3 MKT-116-3 MKT-116-3 MKT-116-5 MKT-116-5 MKT-116-5 MKT-116-5 MKT-1-6 MKT-							unt unt unt unt unt unt unt murtaret murtaret murtaret murtaret murtaret unt unt unt unt unt unt unt unt unt un	27097 32124 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 2751 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	10786 12609 111 0 1789 988 0 148 0 1239 1070 0 1223 0 1298 1099 813 1298 0 9465	5681 10417 1768 3318 1899 2679 2679 4624 1949 323 3886 2090 1613 708 10679 4103 1893 1293 1893 1893 1893 1893 1893 1893 1893 18	674 476 4464 7970 3247 7616 52 2376 3254 3867 3867 11856 6721 13755 2575 1472 3254 3254 3254 3254 3254 3254 3254 325	1962 297 113 0 0 267 0 1143 0 181 0 0 0 800 870 0 0 1759 211 1551 0	963 24 0 0 0 246 302 513 435 0 0 365 689 284 746 199 0 0	483 0 0 0 0 0 0 0 0 0 0 0 0 0
MK pps A+ NFC-116-3 NFC-116-3 NFC-116-3 NFC-116-4 NFC-116-4 NFC-116-5 NFC-116-5 NFC-116-5 NFC-1-6 NFC-							unt unt unt unt unt unt unt unt mutami mutami mutami mutami mutami mutami mutami mutami mutami mutami mutami unt unt unt unt unt unt unt unt unt unt	27097 22124 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	10788 12609 117 12609 117 12609 117 127 1270 1270 1270 1270 1270 1270 1	5681 (0417 1768 3318 1899 2679 1994 4624 1949 320 3886 2090 1613 708 2090 4103 1869 1292 1292 4103 4103 4103 4103 4103 4103 4103 4103	674 478 4464 7970 3247 7618 52 276 3234 3867 11856 8721 13759 2575 1782 2575 1772 3256 3234 36721 13759 2772 13759 2773 1772 3773 1772 3773 1772 3773 1772 3773 1772 3773 1772 3773 3773	1962 297 113 0 0 757 0 1143 0 181 0 0 800 870 0 1759 211 1551 0 414	903 24 0 0 246 302 513 435 0 0 0 0 1055 689 3849 284 1095 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	483 0 0 0 0 0 0 0 0 0 0 0 0 0
MK pps A+ MKT-116-3 MKT-116-3 MKT-116-3 MKT-116-3 MKT-116-5 MKT-116-5 MKT-116-5 MKT-116-5 MKT-13-6 MKT-1-6 MKT							unt unt unt unt unt unt unt mutann mutann mutann mutann unt unt unt unt unt unt unt unt unt u	27097 22124 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 281 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	10786 12609 12609 12609 1101 111 110 1280 0 0 12709 1070 0 0 12709 1070 1070 1070 1070 1070 1070 1070 1	5861 (04)77 1768 3318 1599 2879 2879 2879 2879 320 1949 320 1949 1949 1949 1950 1950 1950 1950 1950 1950 1950 195	674 4788 4464 4464 77818 3247 7618 523 7875 2276 3224 3677 1856 1725 1725 1725 1725 1725 1725 1725 1725	1862 297, 113, 0 0, 0 257, 113, 0 0, 0 113, 0 0, 0 1143, 0 0, 0 0, 0 0, 0 1759, 0 0, 0 0, 0 1759, 0 0, 0 0, 0 0, 0 1759, 0 0, 0 1759, 0 0, 0 1759, 0 0, 0 1759, 0 0, 0 1759, 0 0, 0 1759, 0 0, 0 0, 0 0, 0 0, 0 0, 0 0, 0 0, 0	903 24 0 0 246 302 245 302 91 91 91 91 92 93 94 95 96 99 98 99 90 90 90 90 90 90 90 90 90	483 0 0 0 0 0 0 0 0 0 0 0 0 0
MK pps A+ MKT-116-3 MKT-116-3 MKT-116-3 MKT-116-3 MKT-116-5 MKT-116-5 MKT-116-5 MKT-116-5 MKT-116-5 MKT-1-6 MK							unt unt unt unt unt unt unt unt unt unt	27097 22124 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	10788 12899 12899 12899 12899 12899 1289 128	5881 (0417) 1768 1788 1899 2779 2779 4624 1949 3236 2090 1613 1613 1708 1627 1629 1629 1629 1629 1629 1629 1629 1629	674 478 4464 7970 3247 7818 52] 7875 2276 3234 3677 1956 6721 1956 2255 2255 2255 2255 2256 2257 2257 22	1902 2977 297 1133 0 2577 0 20 1134 0 20 1014 1143 0 20 1014 1143 0 20 0 20 0 211 150 0 211 150 0 214 540 0 2 2 2 2 2 3 3 4 3 4 3 4 3 4 3 4 3 4 3 4	963 24 0 0 0 245 502 513 435 0 363 1055 669 3849 264 746 109 0 0 0 0	483 0 0 0 0 0 0 0 0 0 0 0 0 0
MK pps A+ MKT-116-3 MKT-116-3 MKT-116-3 MKT-116-4 MKT-116-5 MKT-116-5 MKT-116-5 MKT-116-5 MKT-12-3 BVX6 MKT29-4 MKT29-5 MKT29-5 MKT29-6 MKT2							unt unt unt unt unt unt unt mutann mutann mutann mutann unt unt unt unt unt unt unt unt unt u	27097 22124 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	10786 12609 12609 12609 1101 111 110 1280 0 0 12709 1070 0 0 12709 1070 1070 1070 1070 1070 1070 1070 1	5861 (04)77 1768 3318 1599 2879 2879 2879 2879 320 1949 320 1949 1949 1949 1950 1950 1950 1950 1950 1950 1950 195	674 478 4464 4784 4464 7970 3247 7816 52 276 2276 2276 2376 5775 5775 5775 5775 5775 5775 5775 5	1992 297 1133 0 0 757 757 0 0 1143 1143 181 11 191 115 115 115 115 115 115 115 115	993 24 0 0 24 0 0 246 302 513 455 9 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	483 0 0 0 0 0 0 0 0 0 0 0 0 0
MK pps A+ MKT-116-3 MKT-116-3 MKT-116-3 MKT-116-3 MKT-116-5 MKT-116-5 MKT-116-5 MKT-116-5 MKT-1-6							unt unt vet vet vet mutanni mutanni mutanni mutanni vet vet vet vet vet vet vet vet vet vet	37097 32124 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	10786 12609 1110 111 111789 111 1189 100 100 100 100 100 100 100 100 100 10	5881 (9417) 1768 1978 1978 1979 1979 1979 1979 1979 197	674 478 4464 7970 3247 7816 52 276 2276 2276 5079 11654 6721 13755 2575 1572 2575 1572 2419 1525 2575 1572 2419 1525 2419 2419 2577 2419 2419 2419 2419 2419 2419 2419 2419	1992 297 113: 113: 113: 114: 114: 114: 114: 114:	983 983 983 983 983 983 983 983 983 983	483 0 0 0 0 0 0 0 0 0 0 0 0 0
MK pps A+ MKT-116-3 MKT-116-3 MKT-116-3 MKT-116-3 MKT-116-5 MKT-11							set set set set set set set set set set	27097 22129 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	10786 12809 12809 12809 12809 111 0 1789 598 60 148,6 10 1293 1070 0 1293 1070 100 1293 1507 100 1507 100 1507 100 1507 100 1507 100 100 100 100 100 100 100 100 100 1	5881 (0417) 1768 318 8 1899 2791 2201 4624 1949 3222 3886 2004 1913 1013 1013 1013 1013 1013 1013 1013	674 472 4464 7970 3347 7970 52, 275 2276 3867 5872 11856 6721 13755 2280 0 0 1720 1831 1832 1832 1832 1832 1832 1832 1832	1992 297 113. 0. 197 114. 114. 114. 116. 0. 0. 0. 1759 211. 115. 0. 0. 1759 211. 115. 0. 0. 0. 1759 211. 115. 0. 0. 1759 21. 115. 0. 1759 1759 1759 1759 1759 1759 1759 1759	69.1 69.1 69.1 69.1 69.1 69.1 69.1 69.1	483 0 0 0 0 0 0 0 0 0 0 0 0 0
MK pps A+ MKT-116-3 MKT-116-3 MKT-116-3 MKT-116-3 MKT-116-5 MKT-116-5 MKT-116-5 MKT-116-5 MKT-1-6							set set set set set set set set set set	27097 22129 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	10786 12809 12809 12809 1110 0 1782 5988 100 0 1283 1277 0 1203 1203 1203 1203 1203 1203 1203 12	5881 (0417) 1768 1318 1859 2701 2701 1859 2702 1858 2003 1853 1867 1867 1867 1867 1867 1867 1867 1867	674 478 4464 4784 4484 4787 3247 7970 3247 591 591 597 2276 5979 11056 6722 1275 2275 2275 2275 2275 2275 2275 2	1902 2977 1132 0 2977 1132 0 2977 1143 0 1143 0 800, 0 800, 17559 2711 150, 0 414 444 540, 540, 540, 540, 540, 540, 540,	693 693 693 693 693 693 693 693 693 693	483 0 0 0 0 0 0 0 0 0 0 0 0 0
MK pps/A+ MKT-116-3 MKT-116-3 MKT-116-3 MKT-116-4 MKT-116-4 MKT-116-5 AS61-6 MT29-3 BVX-6 MT29-3 BVX-6 MT29-3 GVX-6 MT29-5 GVX-6 MT29-5 GVX-6 MT29-5 GVX-6 MT29-5 GVX-6 MT29-5 GVX-6 MT29-5 GVX-6 MT29-6 GVX-6 MT29-6 GVX-6 MT29-6 GVX-6 MT29-6 GVX-6 MT29-6 GVX-6							set set set set set set set set set set	37097 32124 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	000000000000000000000000000000000000000	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	10786 12809 12809 12809 12809 111 0 1789 598 60 148,6 10 1293 10701 0 1293 1293 1293 1294 1313 1296 1313 1296 1313 1297 1313 1296 1313 1297 1313 1297 1313 1297 1313 1297 1313 1297 1313 1297 1313 1297 1313 1297 1313 1313 1313 1313 1313 1313 1313 13	5881 (0417) 1768 318 8 1899 2797 2201 4624 1949 3222 3886 2000 1813 708 3034 1937 1947 4103 1867 2000 1877 2000 1878 2000 2000 2000 2000 2000 2000 2000 2	674 478 4484 4787 47970 3347 7916 55 324 324 3677 5979 11956 6721 12755 2275 1275 2275 2275 2275 2275	1962 297 113 0 0 287 0 0 143 143 0 0 0 0 0 0 0 0 0 0 0 0 0 181 1 0 0 0 0	893 893 993 995 995 995 995 995 995 995 995 9	483 0 0 0 0 0 0 0 0 0 0 0 0 0
MK pps A+ MKT-116-3 MKT-116-3 MKT-116-3 MKT-116-3 MKT-116-5 MKT-116-5 MKT-116-5 MKT-116-5 MKT-116-5 MKT-1-6 MK							set set set set set set set set set set	27097 22122 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	10786 12809 12809 12809 1110 0 1782 5988 100 0 1283 1277 0 1203 1203 1203 1203 1203 1203 1203 12	5881 (0417) 1768 1318 1859 2701 2701 1859 2702 1858 2003 1853 1867 1867 1867 1867 1867 1867 1867 1867	674 478 4464 4784 4484 4787 3247 7970 3247 591 591 597 2276 5979 11056 6722 1275 2275 2275 2275 2275 2275 2275 2	1902 2977 1132 0 2977 1132 0 2977 1143 0 1143 0 800, 0 800, 17559 2711 150, 0 414 444 540, 540, 540, 540, 540, 540, 540,	693 693 693 693 693 693 693 693 693 693	483 0 0 0 0 0 0 0 0 0 0 0 0 0
MK pps/A- MCT-116 - 3 MCT-116 - 3 MCT-116 - 3 MCT-116 - 4 MCT-116 - 5 MCT-116 - 5 MCT-116 - 6 MCT-2 - 3 MCT-2 - 5 MCT-2 - 6 MCT-2 - 6 MCT-2 - 6 MCT-2 - 6 MCT-2 - 6 MCT-3 - 7 MC							set set set set set set set set set set	77097 32122 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	10786 12609 1110 01189 1110 01896 000 12739 10770 000 12739 10770 000 12839 12939 12	5861 (0417) 1766 1899 1899 1899 1899 1899 1899 1899 18	674 478 4464 4787 4464 477 3447 777 50 327 327 50 327 50 327 50 327 50 327 50 327 50 327 50 327 50 327 50 327 50 327 50 327 50 327 50 327 50 327 50 327 50 50 50 50 50 50 50 50 50 50 50 50 50	1962 297 113 0 0 587 0 1143 0 0 100 270 270 275 0 0 1759 2759 2759 2759 2759 2759 2759 2759 2	983 983 983 983 983 983 983 983 983 983	483 0 0 0 0 0 0 0 0 0 0 0 0 0
MK pps A+  MKT-116-3  MCT-116-3  MCT-116-4  MCT-116-5  MCT-116-5  MCT-116-5  MCT-116-5  MCT-116-5  MCT-116-5  MCT-116-5  MCT-116-5  MCT-1-6  MCT-1-							set set set set set set set set set set	77097 22124 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	10786 12809 1110 0 1789 988 140 0 1299 1209 1209 1209 1209 1209 1209 1	5881 (0417) 1768 1979 2201 6224 1943 2202 1943 2000 2000 10079 100	874 473 4464 4747 4757 4777 4777 4777 4777 4777	1862 2977 1113 0 977 0 101 0 101 101 101 101 101 101 101 101	693 693 693 693 693 693 693 693 693 693	483 0 0 0 0 0 0 0 0 0 0 0 0 0
MK pps A+  MKT-116-3  MCT-116-3  MCT-116-4  MCT-116-5  MCT-116-5  MCT-116-5  MCT-116-5  MCT-116-5  MCT-116-5  MCT-116-5  MCT-116-5  MCT-1-6  MCT-1-							set set set set set set set set set set	170s/ 3212 20 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	10786 12809 1110 01789 111789 1416 140 140 140 140 140 140 140 140 140 140	5861 (0417) 1766 1890 1890 2790 280 280 280 280 280 280 280 280 280 28	874 478 4464 1770 3347 7700 3347 7810 3274 3274 3367 11854 8721 11854 8721 12755 2275 1275 2275 1275 2275 2275	1862 297 113 30 00 00 10 10 10 10 10 10 10 1	683   24   24   2   2   2   2   2   2   2	483 0 0 0 0 0 0 0 0 0 0 0 0 0
MK pps/A- MKT-116-3 MKT-116-3 MKT-116-3 MKT-116-3 MKT-116-5 MKT-116-5 MKT-116-5 MKT-116-5 MKT-116-5 MKT-116-5 MKT-116-5 MKT-116-5 MKT-116-5 MKT-116-5 MKT-116-5 MKT-116-5 MKT-116-6 MKT-11							set set set set set set set set set set	77097 22124 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	10786 12809 1110 0 1789 988 140 0 1299 1209 1209 1209 1209 1209 1209 1	5881 (0417) 1768 1979 2201 6224 1943 2202 1943 2000 2000 10079 100	674 4783 4464 17707 1707 1707 1707 1707 1707 1707 17	1962 2977 1113 0 977 1019 1019 1019 1019 1019 1019 1019 1	683   683   7	483 0 0 0 0 0 0 0 0 0 0 0 0 0
MK pps/A+ NFC-116-3 NFC-116-3 NFC-116-3 NFC-116-3 NFC-116-3 NFC-116-4 NFC-116-5 NFC-116-5 NFC-116-5 NFC-116-5 NFC-1-6							unt unt unt unt unt unt unt unt unt unt	### 1709/ #### 1709/ ### 1709/ ### 1709/ #### 1709/ #### 1709/ ### 1709/ ### 1709/ #### 1709/ #### 1709/ #### 1709/ ####################################	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	10786 12609 11 17 11 18 18 18 18 19 19 19 19 19 19 19 10 10 10 10 10 10 10 10 10 10 10 10 10	5861 (0417) 1768 1992 1992 1992 1992 1993 1993 1993 1993	674 4783 4464 17770 17700 1780 1780 1780 1780 1780 17	1862 297 113 30 00 00 10 10 10 10 10 10 10 1	863   863   70   70   70   70   70   70   70   7	483 0 0 0 0 0 0 0 0 0 0 0 0 0
MK pps A- MKT-116-3 MKT-116-3 MKT-116-3 MKT-116-3 MKT-116-5 MKT-116-5 MKT-116-5 MKT-116-5 MKT-116-5 MKT-116-5 MKT-116-5 MKT-116-5 MKT-1-6 MKT-							iet in de de de de de de de de de de de de de	170s/ 21124 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	10786 12609	5861 10017 1769 1769 1769 1769 1769 1769 1769 17	674 473 4464 474 478 4464 478 4464 478 478 4864 478 478 478 478 478 478 478 478 478 47	1862 297 1113 0 0 167 100 100 100 100 100 100 100 100 100 10	693   693   24   693   6	483 0 0 0 0 0 0 0 0 0 0 0 0 0
MK pps/A- MKT-116-3 MKT-116-3 MKT-116-3 MKT-116-3 MKT-116-4 MKT-116-4 MKT-116-5 AS41-6 MKT-2-3 BKYX-6 MKT29-3 BKYX-6 BKYX							iet ind, ind ind ind ind ind ind ind ind ind ind	### 1709/ #### 1709/ ### 1709/ ### 1709/ #### 1709/ #### 1709/ ### 1709/ ### 1709/ #### 1709/ #### 1709/ #### 1709/ ####################################	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	10786 12609 1110 1110 1189 1289 12809 1480 0 1273 1070 1070 1070 1070 1070 1070 1070 10	5861 (0417) 1766 1766 1890 1890 1890 1890 1890 1890 1890 1890	674 478 4464 478 4464 478 4464 478 48464 478 48464 478 48464	1862   18	683   683   241	483 0 0 0 0 0 0 0 0 0 0 0 0 0
MK pps A+  MK pps A+  MK ps						iet in de de de de de de de de de de de de de	170s/ 21124 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	10786 12609 1110 1110 1189 1289 12809 1480 0 1273 1070 1070 1070 1070 1070 1070 1070 10	5861 10017 1769 1769 1769 1769 1769 1769 1769 17	674 473 4464 474 478 4464 478 4464 478 478 4864 478 478 478 478 478 478 478 478 478 47	1862 297 113 0 97 113 103 103 103 103 103 103 103	693 693 693 693 693 693 693 693 693 693	483 0 0 0 0 0 0 0 0 0 0 0 0 0	
MK ppty A+ NFC-116-3 NFC-116-3 NFC-116-3 NFC-116-3 NFC-116-3 NFC-116-4 NFC-116-4 NFC-116-5 NFC-1							ed ed, ed, ed, ed, ed, ed, ed, ed, ed, e	### ##################################	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0   0   0   0   0   0   0   0   0   0	10786 12609 11 10 10 10 10 10 10 10 10 10 10 10 10	5861 (0417) 1768 1768 1899 320 4624 1899 320 3386 5090 1913 3386 1913 3386 1913 3386 1913 3386 1913 3386 1913 3386 1913 3386 1913 3386 1913 1913 1913 1913 1913 1913 1913 191	674 478 4464 478 4464 478 4664 478 478 478 478 478 478 478 478 478 47	1862   18	683   24   24   24   25   25   25   25   25	
MS pery A-  MS pery A-  MS Table A-  MS Tabl							uel  ed,  ed,  ed,  ed,  ed,  ed,  ed,  ed,	77097 20122 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0		0   0   0   0   0   0   0   0   0   0	10786 12609	\$681 10017 1760 3102 2779 2779 2779 3280 3004 1007 3007 3007 3007 3007 3007 3007 3007	674 478 4464 478 4664 478 4664 478 478 478 478 478 478 478 478 478 47	1862   18	683   24   24   2   2   2   2   2   2   2	
MK pps/A- MKT-116-3 MKT-116-3 MKT-116-3 MKT-116-3 MKT-116-3 MKT-116-4 MKT-116-4 MKT-116-5 AS60-6 MKT29-3 BKYX-6 MKT29-3 BKYX-6 MKT29-3 GKYX-6 MKT29-5 GYCAR4-6 GYCAR4-6 GYCAR4-6 GYCAR4-6 GYCAR4-6 GYCAR5-6 MK-7-6 M							ind  ind  ind  ind  ind  ind  ind  ind	### 1709/ #### 1709/ ### 1709/ ### 1709/ #### 1709/ #### 1709/ ### 1709/ ### 1709/ #### 1709/ #### 1709/ #### 1709/ ####################################	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0   0   0   0   0   0   0   0   0   0	10786 12609 11 17 17 18 18 18 18 18 18 18 18 18 18 18 18 18	\$601 (0017) 1768 1768 1899 1899 1999 1999 1999 1999 1999 19	674 478 4464 478 4464 478 4464 478 478 478 478 478 478 478 478 478 47	1862   18	883   883   241   90   90   90   90   90   90   90   9	
MK pps/A- MK pps							est with the second sec	77097 20122 20122 20222	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	10786 12609	\$681 10017 1780 3782 2791 2791 3806 6 3004 3004 3004 3004 3004 3004 3004	674 473 4464 473 4464 474 478 4464 478 478 478 478 478 478 478 478 478 47	1862   18	683   24   24   2   2   2   2   2   2   2	
MK pps A- MKT-116-3 MKT-116-3 MKT-116-3 MKT-116-3 MKT-116-3 MKT-116-5 MKT-11							ind  ind  ind  ind  ind  ind  ind  ind	### 1709/ #### 1709/ ### 1709/ ### 1709/ #### 1709/ #### 1709/ ### 1709/ ### 1709/ #### 1709/ #### 1709/ #### 1709/ ####################################	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0   0   0   0   0   0   0   0   0   0	10786 12609 11 17 17 18 18 18 18 18 18 18 18 18 18 18 18 18	\$601 (0017) 1768 1768 1899 1899 1999 1999 1999 1999 1999 19	874 4783 4464 4787 4787 7777 7875 7876 3224 3257 5972 11072	1862   18	683   241   241   242   241   242   241   242	
MS pery A+  MS pery A+  MS Test A+  MS Tes							est with the second sec	### 1709/ #### 1709/ #### 1709/ #### 1709/ #### 1709/ #### 1709/ #### 1709/ ####################################	0	0   0   0   0   0   0   0   0   0   0	10786   10786   12609   1260	\$661 10017 1766 33162 2679 2679 3221 1989 3223 1983 3234 1987 1987 1987 1987 1987 1987 1987 1987	674 478 478 466 478 466 478 478 478 478 478 478 478 478 478 478	1862   18	683   24	
MS pery A+  MS per							est with the second sec	### ##################################		0   0   0   0   0   0   0   0   0   0	10786 12609 11 10 10 10 10 10 10 10 10 10 10 10 10	\$681 (0417) 1768 1768 1899 1899 1899 1899 1899 1899 1899 18	674 478 4464 478 4464 478 4464 478 4664 478 478 478 478 478 478 478 478 478 47	1862   18	683   241   241   242   242   243   244   245	
MS pery A-  MS per							est with the second sec	### ### #### #########################		0   0   0   0   0   0   0   0   0   0	10786 12609	\$681 10017 1766 3716 2779 2779 2779 3780 3886 3004 1007 3886 3004 1007 3886 3004 1007 3004 1007 3004 1007 3007 4103 3004 1007 3004 1007 3007 3007 3007 4103 5007 4103 5007 4007 4007 4007 4007 4007 4007 4007	674 478 4464 478 4664 478 4664 478 4664 478 478 478 478 478 478 478 478 478 47	1862   1862   1862   1863   18	683   24	
MS per A :  MS per							est with the second sec	### ##################################		0   0   0   0   0   0   0   0   0   0	10786 12609 11 10 10 10 10 10 10 10 10 10 10 10 10	\$661 (0417) 1768 1768 1899 320 4624 1999 320 4624 1999 320 4624 1999 320 4624 1999 4103 1999 4103 1999 4103 1999 4103 1999 4103 1999 4103 1999 4103 1999 4103 1999 4103 1999 4103 1999 1999 1999 1999 1999 1999 1999 1	674 478 4464 478 4464 478 4464 478 4664 478 478 478 478 478 478 478 478 478 47	1862   18	863   863   241   261	
MS pery A+  MS pery A+  MS Test A+  MS Tes							est with the second sec	### ##################################		0   0   0   0   0   0   0   0   0   0	10786 12609	\$681 10017 1766 3716 2779 2779 2779 3780 3886 3004 1007 3886 3004 1007 3886 3004 1007 3004 1007 3004 1007 3007 4103 3004 1007 3004 1007 3007 3007 3007 4103 5007 4103 5007 4007 4007 4007 4007 4007 4007 4007	674 478 4464 478 4664 478 4664 478 4664 478 478 478 478 478 478 478 478 478 47	1862   18	683   24	
MS poly A-  MS poly A-  MST-118 - 4  MST-118 - 4  MST-118 - 4  MST-118 - 4  MST-118 - 4  MST-118 - 4  MST-118 - 5  MST-118 - 5  MST-118 - 6  MST-118							est with the second sec	### ### ### ### ### ### ### ### ### ##		0   0   0   0   0   0   0   0   0   0	10786 12609	\$681 10017 1760 3718 2001 2001 2001 3806 3806 3806 3806 3806 3806 3806 3806	674 473 4464 473 4464 474 478 4464 478 4664 478 478 486 478 478 478 478 478 478 478 478 478 478	1862   18	693   693   7   7   7   7   7   7   7   7   7	
MS pery A-  MS per							est with the second sec	### 1709/ #### 1709/ #### 1709/ #### 1709/ #### 1709/ #### 1709/ ####################################	O   O   O   O   O   O   O   O   O   O	0   0   0   0   0   0   0   0   0   0	10786   10786   12609   1260	\$661 10017 1760 31162 2779 2779 3223 36824 1989 3223 1987 3034 1987 1987 1987 1987 1987 1987 1987 1987	674 478 478 466 478 466 478 478 478 478 478 478 478 478 478 478	1862   18	683   24	
MK ppty A-1 MK ppty A-1 MKT-116 - 3 MKT-116 - 3 MKT-116 - 4 MKT-116 - 4 MKT-116 - 4 MKT-116 - 5 MKT-116 - 5 MKT-116 - 5 MKT-116 - 5 MKT-116 - 6 MKT-116 - 5 MKT-116 - 6 MKT-11							est with the second sec	### ### ### ### ### ### ### ### ### ##		0   0   0   0   0   0   0   0   0   0	10786 12609 11009 11009 12609 12609 12609 12609 1270 1270 1270 1270 1270 1270 1270 1270	\$661 10017 1760 1760 1760 1760 1760 1760	674 473 4464 473 4464 473 4464 473 4464 474 475 477 477 477 477 477 477 477 47	1862   18	683   24	
MK ppty A-1 MK ppt							est with the second sec	### 1709/ #### 1709/ #### 1709/ #### 1709/ #### 1709/ #### 1709/ ####################################	O   O   O   O   O   O   O   O   O   O	0   0   0   0   0   0   0   0   0   0	10786   10786   12609   1260	\$661 10017 1766 3116 277 277 277 277 277 277 277 277 277 27	674 478 478 466 478 466 478 466 478 478 466 478 478 478 478 478 478 478 478 478 478	1862   18	683   24	
MK pps A -							est with the second sec	### ### ### #### #### ################	O   O   O   O   O   O   O   O   O   O	0   0   0   0   0   0   0   0   0   0	10786   10786   12609   1260	\$681 10017 1760 3716 2779 3780 3780 3880 3880 3890 3890 3890 3890 3890 38	674 478 4464 478 4464 478 4464 478 4664 478 4864 478 4864 478 4864 478 4864 478 4864 478 4864 478 4864 478 478 478 478 478 478 478 478 478 47	1862   1862   1862   1863   18	683   241	
MK pps/A-  MK pps/A-  MKT-116 - 3  MKT-116 - 3  MKT-116 - 4  MKT-116 - 4  MKT-116 - 5  MKT-116 - 6  MKT-1 - 6  MKT-1 - 6  MKT-2 - 3  EVX 6  MKT-2 - 3  EVX 6  MKT-2 - 3  EVX 6  MKT-2 - 3  EVX 6  MKT-2 - 3  EVX 6  MKT-2 - 3  EVX 6  MKT-2 - 3  EVX 6  MKT-2 - 3  EVX 6  EVX 6  MKT-2 - 3  EVX 6  EVX 6  EVX 6  EVX 7  EVX 7  EVX 7  EVX 8  EVX 8  EVX 8  EVX 8  EVX 8  EVX 9  EVX.							est with the second sec	### ### #### #########################		0   0   0   0   0   0   0   0   0   0	10786 12609 11 1000 12609 11 1000 1000 1000 1000 1000 1000 100	\$661 10017 1768 1768 1970 1970 1970 1970 1970 1970 1970 1970	674 478 4464 478 4464 478 4464 478 4664 478 478 478 478 478 478 478 478 478 47	1862   18	863   863   241   241   261	

Table 3 (contd)

	-															
Tiesue actense gland - h	1 umor-sym	Normel-sym	Tumor - 1a	Tumor cella	Normal	Endos	P53	SEQ 644	TREEQ 45	ANSEQ 47	WSEQ 4	AASEQ 49	AN SEG 51	CIÁSEO 52	ANSED S4 C	CSEQ 15 C
lymph nade - h	+	1 2	+	<del></del>	+	+	+-	106 25	18			68 78 84 85	151 22 74 71	53 17	92: 2026; 70: 779:	2: 37691
bone merow - h		. 3						19	68		17	0 56	53 38	16 13	70 7791 81 111	
manmary gland - h		- 4							41		0	0 27				0 325
percrese - h	+	6	+	+		+	+	46			39 2	30 64	95 8	9 9	87 1195	
cerebelum - h		7		<del>                                     </del>	-	+		86	58 i		0 3	44 70 0 76		12 8	98 872	
producy gland - h	4	8						108				31 85	281 65	36 31 97 9	89 13785 32 32295	
fetal brain - h	<del> </del>	9	+	<del></del>		-	$\overline{}$	521		0 2	571	89 77	13 56	14 30		
placents - h fetal kidney - h	<del> </del>	10	+	+		+	+-	23			11	871 810	3 23	50 23	12 41090	0 35806
proptate, h		12		1		1.	<u> </u>	20		0 2	4	0 93		13	75 30344 34 5551	
fetal liver- h		13						29	78	0 1		50 53±			10 4385	
estvery at h	<del></del>	14	+				1		0	0 1	ю	0 290	34	8 11		1 26923
fetal lung - h ekeletal muscle - h	<del></del>	16	<del></del>	+	+		+	325		0 3	9 3	46 107	3 63	179	58 20642	2 64752
heart - h		17		<del>                                     </del>	+	+-	_	64		0	0 1	D 570				
email intentrio - h		18						279		0 1	6 1	44 700			22 2810 43 4172	
lodney - It epinel cold - It	+	19		<b>↓</b>			1			0 18	1 2	25 634	200	2 76	61 7039	
liver - h	<del>                                     </del>	20		+	+	+	<del></del>	834		0 13	G G	0 567	9 264	6 5	58 1254	14331
Splann - h		22	<del></del>		1	1	1	ZX				0 481	7 330	0 8	33 0 31 997	
lung - h		23	1					201			5 1	77 396				
etomach -h tents - h	<del> </del>	24	<del></del>	<del> </del>	+			268		0 12	5	0 380	81	2 20	1243	
thymus dr	<del> </del>	25 27		<del> </del>	-	-	+-	120		0 116		00 56	82			
HPAEG.		26			-	. 28	-	3				23 619 35 535			0 11408	
thyroid gland - h	<u> </u>	29	1					80		0 15	a	0 530			56 8454	
RPTEC traches - h	<del></del>	30	+	<del> </del>	+	30	-	16			9	98 418	1074	4 6	541 0	01 8460
HMEC	_	32		<del> </del>	+	+	+	341		0 7	9	01 616	2 415			
utenus - h		33		<del> </del>		+	<del>                                     </del>	398		0 3		38 440 07 725			19 393	
HCAEC	<del> </del>	34	1	$\vdash$	T	<b></b>		16	4	0! 2	6	ro 575	1 683	5 21	551 7394 19 661	
Pancrees - h	<del> </del>	35	+	<del> </del>	+	+	+-	57		0	0!	0 628	8	o:	0; 17	7 21419
hengih nade - h Skeletel muecie - h	<del>                                     </del>	37	+	<del> </del>	+	+	+	151		0 11		0 537		4 11	9607	
latel boar- h		38						603	5			0 341 0 688	1 907	0 3 2 13	0 M	
Heart - h	<del> </del>	39	+		· · · · · · · · · · · · · · · ·	$\perp =$		96	8	0 1	7 :	406	5] 1080	4	4 0	
drymus.h Duodenum - h	1	40	+	+	+	+	1	10			01 9	7 463	3 875	j]	0 0	26458
Feta bran - h		42		-	1	1	1	1182			0	0 305	9 920	0 14	0 0	
Salvary ol h		43	<b></b>				$\vdash$		0	0	0 40	7 551	1 142	14	8 6	
HT218-normal			+		1	+	$\vdash$	173	2	0 2	7: :	744	4 1956	2 11	5 12733	
HT213-norms	<del> </del>	<del> </del>	+	<del></del>	365	+	+	67	0			0 30	1	0	0 0	0
HT157-narmal		L			361		+	219				0 29			2 0	
Ber-13		ļ			356	356		510	0	0	9 40	3 869				
Ber-12 carebatum - h		+	<del> </del>		354 344	354	+	502	7	0 4		0 540		5 31	6 330	2524
bren -h			1		342	1 .	1	+		0 7		0 196			0 360 D 298	: 6728
RPTEC			<b></b>		334	334			0	0	3 20	0 162			0 298	
hymph node - h	⊢——	+	<del> </del>		332	_		271	4	0	5	0 403	41	52	11 0	27619
h adult SMC 19/21/92 #17 Fetal brain - h	1	<del>                                     </del>	<del> </del>		330	+	+		2			6 448		8		551
HT396-normal					327		1	352		0 25		0 708 6 485			3 4350 0 42	
thymus,h	$\vdash$				326			291	2	0	25			62		
HT149 - normal	——		<del></del>		321		T	24	8	0	3	0 345			0 0	
HEPM 3d untremed wheree • h	t	<del>                                     </del>	+	<del> </del>	320	+	+	144 352		0 31		6 382 0 633			0 0	3657
traches - h					316	1	<u> </u>	142	-	0 31	15				7 5551	
thread gland - h		<b></b>			314		$\Gamma$	380	0	0 22	17	5 527	2 44	38	3 5888	
ealwary gl h prostate, h	<del>                                     </del>	<del>                                     </del>	<del> </del>	<del> </del>	311	<del> </del>	$\overline{}$	23		0 6	k}	5050	811	2	7 0	17721
pitulary gland - It					307	-	1	- 29		0	37	0 5456 0 3426				
parcram - h					305	$\vdash$		1		0 3	25	513	226	54		
mammery gland - h blander - h		<del>                                     </del>	<del></del>	<u> </u>	303			364		0 36	! 3	5370	4079		0 0	37185
100120 - h		<del></del>	<del> </del>		298	+	<del> </del>	9310		0 370	10		167			
iver - h					297	<b>1</b>	<u> </u>	385			41	4 9504	1291			
Spiesn - h epinal cord - h		<del> </del>	<del> </del>		296	1		241		0 114		3615	3035		462	
email intestine - h			<del> </del>		294 292	┼	-	22		0 84		593		30	543	
skeistel muscle - h			1		290	<del> </del>	1	1380		245		5290	657	176	5 824	
bone martow - h			$\downarrow = $		279			T		88 10		5448	116			
estremet gland - h HPAEC			-		277			185				4734	1197		1346	
HT392-normal			<del></del>		275 268	275	+	1 - 5		0 41		3704			0	
HT382-normal					266			129		<del>                                     </del>				349	0 474	
Bev-11					239	239			) (		8	7954			1621	13792
HT372-normal	<del></del>	<del> </del>	<del> </del>		235 234	235	<del> </del>	80		154		4062	560	1. 0	52	4552
Bes-7					233	233	<del>                                     </del>	675		3 47		6155				2457
Bev-6	$\vdash$		Į		Z31	231			10	130						
Bev-2 Bev-1	<b></b>		-		229	229	+===			36 80	16	3519	4889	152	0	6168
bladder - h		<del>                                     </del>			227 222	227		<del>}</del>		907		3 2450			) ( C	4163
Heart - h					215			16777		0				53	454	
stomach -h			4		214			1496		41	14.	8056	1680		1381	
fetal Iver- h placente - h	<del></del>	<del></del>	<del>                                     </del>		213		<del> </del>	1346		90			1 0	133	31 0,	12002
HCAEC					212	211	r—	1246		3 - 8		5011				
fetel bran - h					210			4492				5900				
HMEC Duodenum - h		<del></del>	$\vdash$		209	$\vdash$		39	1)	11		2824	3235	36	596	316
Skeletal muscle - h					205 203		<del>                                     </del>	5184 1310					. 0		<u>. 1</u>	3834
Pancreas - h					201			752	- 0	29		3179				278 4188
Selvery pl h					199			206		15		2838	0		0	12559
Selvery gl h HEPM 3d TGFB1 detergent+DNesse			<del> </del>		197 195			160		15		2207		52	4299	22443
enymus -h					193			115				1367	174 565	62	23	1613 24671
W1-38 72h					179				0			1150	O	0		
lymph node - h lung - h			<del></del>		61 59	$\vdash$	<u> </u>	447	0	6					0	9800
tadrey - h			<del>                                     </del>		57	$\vdash$		1425 595	0	0			1000	74		
heart - h					55			242	0	64		3084	247			
feld king - h					53			0	0	0		1718	142		537	410
fetal liver- h fetal luciney - h			<del> </del>		51 49			174					361			
HELA-2h-031899				79				0	0	96	70		2158 628			12023 37510
HELA-41-031899								0	0	82		4853	257			
				83 86				143	0	48		5886	4697	. 0	200	1575
HELA-4n-031699				88		<del></del>		596 299	0				0 635		Z31	9984
				90				- 29	0				707	0 583	0	3846 6370
HELA-01-031859 HELA-01-031859 HELA-61-031859 HELA-81-031869								53		70						28215
HELA-0n-031699 HELA-0n-031699 HELA-0n-031699 HELA-0n-031699 HELA-10n-031699				92											0	
HELA-0n-031899 HELA-0n-031899 HELA-0n-031899 HELA-10n-031899 HELA-10n-031899 HELA-11h-031899				94				405				6857	0	239	0	1053
HELA-0n-031899 HELA-0n-031899 HELA-0n-031899 HELA-0n-031899 HELA-10n-031899 HELA-11h-031899 HELA-11h-031899 HELA-11h-031899				92 94 96 146				1639	. 0	99		6857 4356	4121	239 72	0	1053 1789
HELA-0-031699 HELA-0-031699 HELA-0-031690 HELA-0-031690 HELA-0-031690 HELA-0-031690 HELA-0-031690 HELA-10-031690 HELA-10-031690 HELA-10-031690 HELA-10-031690				94 96 146 145			Ξ	1639 86 22	0	99		6857 4356 3197 2154	4121 579 60	239	0 0 5223	1053 1789 6625
KELA-0-031699 KELA-0-031899 KELA-09-031899 KELA-09-031899 KELA-19-031899 KELA-111-031899 KELA-111-031899 KELA-111-031899 KELA-111-031899 KELA-12-031899 KELA-12-031899 KELA-12-031899 KELA-12-031899				94 96 146 148 150			Ξ	1639 86 72 0	0 0	99 0 0 30	0 0 153 0	6857 4356 3197 2154 1847	4121 579 60 1853	239 72 0 143 194	0 0: 5223 1739 759	1053 1789 6625 435 2447
HELA-01-031959 HELA-0				94 96 146 145 150				1639 86 22 0 2072	0 0 0	95 0 0 30	0 0 153 0 347	6857 4356 3197 2154 1847 2204	4121 579 60 1853	239 72 0 143 194 343	0 0 5223 1739 759 3370	1053 1789 6625 435 2447 2928
HELA-6n-031599 HELA-6n-031699 HELA-6n-031699 HELA-6n-031699 HELA-6n-031699 HELA-10-031699				94 96 146 140 150 152 154 156				1639 86 22 0 2072 969	0 0 0 0	95 0 0 30 0 0 42	0 153 0 347 0 247	6857 4356 3197 2154 1847 2204 3623 1822	4121 579 60 1853	239 72 0 143 194 343	0 0 5223 1739 759 3370 6096	1053 1789 6625 435 2447 2928 5502
HELA-0-031659 HELA-0-031659 HELA-0-031659 HELA-0-031659 HELA-0-031659 HELA-10-031659 HELA-031659 HELA-031				94 96 146 148 150 152 154 156 158				1639 86 22 0 2072 989 0	0 0 0 0 0	99 0 0 30 0 0 42 42	0 0 153 0 347 0 247 578	6857 4356 3197 2154 1847 2204 3623 1822 546	4121 579 60 1853 0 1199 0	239 72 0 143 194 243 0 0 539	0 0 5223 1739 759 3370 6096 758	1053 1789 6625 435 2447 2928 5502 1622
HELA-6n-031599 HELA-6n-031699 HELA-6n-031699 HELA-6n-031699 HELA-6n-031699 HELA-10-031699				94 96 146 145 150 152 154 156 158				1639 86 72 0 2072 969 0 0	0 0 0 0 0	95 0 0 30 0 42 42	0 0 153 0 347 0 247 578 140	8857 4356 3197 2154 1847 2204 3623 1822 546 1720	4121 579 60 1853 0 1199 0 0	239 72 0 143 194 243 0 0 539	0 0 5223 1739 759 3370 8096 758 1114	1053 1789 6625 435 2447 2928 5502 1622 0
HELA-6n-031899 HELA-6n-031899 HELA-6n-031899 HELA-6n-031899 HELA-6n-031899 HELA-10n-031899 ELA-10n-03189 HELA-10n-03189 HELA-10n-03189 HELA-10				94 96 146 148 150 152 154 156 158				1639 86 22 0 2072 989 0	0 0 0 0 0	95 0 0 30 0 42 42 92	0 0 153 0 347 6 247 578 140	6857 4356 3197 2154 1847 2204 3623 1822 546 1720 1622	4121 579 60 1853 0 1199 0 0 1178 217	239 72 0 143 194 243 0 0 539	0 0 5223 1739 759 3370 6096 758 1114 0 1036	1053 1789 6625 435 2447 2928 5502 1622

174 Table 3 (contd)

7	10	T6.														
Tinawa Cata I	1 umor sym	Normai-sym	Tumor - to		a Norma	Endos	<b>P53</b>	3EQ 844	TREEQ 45 A	MISEO 47 A	A SEQ 48 A	A SEC 49 A	ASEQ 31 K	ASEQ SI A	45EQ 54 CC	SEQ 35 C
786-0				168	+-		+	401	01	0 4	71 8	8 401	21	15-	258	644
T-47D				169	<b></b>	1			0	0 7	0 21	21 445	6 73	29		2088 718
GRU1441 RNA 8/30	+	<del> </del>	-	171	_	-	_			0	0 2	5 164	5 278			26
781T untreated • DName		<u> </u>	1	183		_	<del> </del>				0 565	2 139				
KB poly A+	+			194	$\neg =$	<b>T</b>			0	0	0 13:	5 165	3 2			789
HOS poly A+			+	198	+	<del></del>	+	28		0 4	8	D 243	7 0	8	B4	378
UACC-62			Ι	200				36	5	0 3:	9 13					316
MCF-7/ADR-RES UTOS (Mandy) poly at	<del></del>	<del> </del>		202		4			Q!	0] 3	6] (	125	7 700		1430	102
WISH (Collegen) poly A+			<u> </u>	206						0 17		74			42	943
458 medulio mRNA CCL,137 RNA 3/21/68	<del></del>			208	$\rightarrow$			584	11 (	0	0 (	713	7 0			119 885
WI-38 72h 0.5%FBS, 24h 10% FBS			<del>                                     </del>	218 219		+-	┼	-		0 80	D 14			100	_ 0	82
CRL1441 + TPA (24h) 8/30			Γ.	220							224	99				89
Ken-2	+	<del></del>		221 223		+	-	68		0	0 16		2! 0		0	125
Ken-4				225 241				73		17	2 0		330		0	133
MOP-92 MOLT-4	<del></del>	<del></del>					-	120	<u> </u>	0 0	<u> </u>	112	377		6	175
BKVX			<del> </del>	242			-	1225	<del>}</del>	0 0		4100	1256		2452	5190
HL-60 NCI-H23				244						01 0		365		217 614	3610 1496	7440
RPM 8226		<del>                                     </del>		245 246		-		231	<u>'                                    </u>	10	183	35.26	1613	221	3362	632
ASSEVATOR				247		1		- 7	<del>                                   </del>	9 80					0	736
SR OVCAR-3				248		4			1		1	2105				2209
HCT-15			<del></del>	249 250		+	├	1042	<del> </del>	17		3481	0	45	163	2209 544
OVCAR-4				251				2		63				293	64 6 890	13641
UO-31 OVCAR-5		·	<del></del>	252 253	+	+		347			56	814	0	Ö	463	1047
SNIZC				254		$\pm$		811		0 69				362	4789	6832
OVCAR-8 LOX IMVI	-			255	$\overline{}$			322		0	13	3581	872	0	2102	6556 1742
IGROV1			<u> </u>	256 257	<del>- i</del>	1		894		94			4990	283	2950	8100
SK-MEL-2				258	1	$\perp$		0		115				338		3937 2004
SK-MEL-5				259	+	+7	$\vdash$	90		. 0	0	1166	0	164	1499	1437
SF-539				261	$\bot$			1273		168	472			0	199	1486 2689
SK-MEL-28 K-562	<del>_                                    </del>			262		-		857 157			0	3750	661	0	2959	2053
UACC-257				264				157			31				2537	1782
M14 MCF7	<b>├</b> ───			265						74		977	151	181	01	1458
MDA-M8-435				267		<del>1 -  </del>		5620 0		60	25				17404	29802
HT279 MDA-N				270	$\perp$			1743	0	0	- 0			67	744	1343
Y79 pay A+	<u> </u>			271 273		+		8005		17		4127	-	293	1252	2025
KHOS paly A •				289				2709			269	7232 3265		264	856	16372
HTB36 24h TPA RNA 6/23 HELA-EXP-031699	$\vdash$			300				0		10	0	2952	546	171	579 66	8284 6378
HTB36 OR RMA				313 322		+		639			49 199	2177 4154	949 566	24	q	10940
HT347 458 medullo RNA				323	4			442		5	0	2446	3812	428 D	169	4214 58352
NCI-HZ26	<del>   </del>			324 336		1		2299				3454	0	. 11	761	1101
HOP-62				337					ő		38 357	2966 3132	301	100	5222	1149
MDA-M6-231 U251				338		$\Box$		7560	•	22	0	8113	4555	0	8554	2879 26931
PT cells poly A-				339		+	-i	19346	- 0		00	11550 1866		202	141693	38706
PC-3 HCC-2998				341				Ò	۰	. 0	227	3570	708	83	2461 584	2005 818
SW-620				343 345	+	<del>  </del>	<del></del> +	31	0			2169	01	139	0;	1570
HT192 COLO 205				346				578	. 0		53 25	2072 4300	509	105	3475	19731
HT218	<del></del>		<del></del>	347 348		$\vdash$	}	0	0		45	703	688	0	0	0
KM-12				349		<u> </u>		4211 0	0				842	102	0	1055 1130
HT151 A490			$\overline{}$	350 351				. 0	0	30	202	3787	1503	299	- 6	9776
HT393						<del>                                     </del>		7849	0		164	1948				
RXF 393 TK-10			1									****	0	200	٥	0
Maime-3M				352 353				0	0	114		6001	0	200	0	18131
	===			353 355	=			5344	0	114	0	9001 2570 7558	0 0 0 2225	200 0 0	0 0 0 3006	0 18131 775 17069
Ha 578T				353				0	0	114 0	0	9001 2570 7558 26180	0 0 2225 15570	200 0 0 0 313	0 0 3006 37531	0 18131 775 17069 7453
			50	353 355 357				0 5344 2845 0	0	114 0 0 0 162	0 0 0	9001 2570 7556 26180 1858 18822	0 0 2225 15570 0 1275	200 0 0 313 0 37	0 0 3006 37531 596	0 18131 775 17069 7453 1109 4385
Ha 578T HT213 HT288 HT139			52 54	353 355 357				0 5344 2845 0 0 195	0000	114 0 0 0 0 162 197	0 0 0 0	9001 2570 7556 26180 1858 18822 5482	0 0 2225 15570 0 1275 437	200 0 0 0 313 0 37	0 0 3006 37531 996 0 429	0 18131 775 17059 7453 1109 4385 48948
He 5787 HT213 HT288 HT189 HT155			52 54 56	353 355 357				0 5344 2845 0 0 195	0 0 0	114 0 0 0 162 197 0	0 0 0 0 0 0	9001 2570 7556 26180 1858 18822 5482 3241	0 0 2225 15570 0 1275	200 0 0 0 313 0 37 0	0 0 3006 37531 996 0 429	0 18131 775 17059 7453 1109 4385 48948 2708
No 578T HT213 HT238 HT139 HT135 HT165 HT161 HT170			52 54 56 56 50	353 355 357				0 \$344 2845 0 0 195 0 0	0 0 0	114 0 0 0 162 197 0 114	0 0 0 0 0 31 0 26	9001 2670 7556 26180 1858 18822 5482 3241 3061 3238	0 0 0 2225 15570 0 1275 437 0 0 588	200 0 0 313 9 37 0 0	0 0 3006 37531 996 0 429 0	0 18131 775 17069 7453 1109 4385 48948 2708 12179 248
N= 574T HT213 HT288 HT139 HT139 HT163 HT163 HT170 HT170			52 54 56 58 60 62	353 355 357				0 5344 2845 0 0 195 0 0 337	0	114 0 0 0 162 197 0 114 35 28	0 0 0 0 0 0 31 0 26	9001 2670 7550 26180 1858 18822 5482 3241 3061	0 0 0 2225 15570 0 1275 437 0	200 0 0 313 0 37 0 0 0	0 0 3006 37531 996 0 429 0 0	0 18131 775 17069 7453 1109 4385 48948 2708 27189 245 12050
he 57AT HT213 HT288 HT188 HT195 HT195 HT195 HT197 HT197 HT197 HT197 HT197 HT197 HT198			52 54 56 56 50	353 355 357				0 5344 2845 0 0 195 0 0 337 0 0	0 0 0 0 0 0 0	114 0 0 162 197 0 114 35 28	0 0 0 0 0 31 26 0	6001 2570 7556 26180 1856 18822 5482 3241 3061 3236 6032 4071 3571	0 0 0 2225 15570 0 1275 437 0 0 508 0	200 0 0 313 0 37 0 0 0 0 0	0 0 0 3006 37531 996 0 429 0 0 0 0	0 18131 775 17069 7453 1109 4385 48948 2708 12179 248 12550 12650 2202 26749
Ne 578T KT213 KT228 KT328 KT155 KT163 KT176 KT172 KT172 KT178 KT178			52 54 56 50 60 62 63 64 65	353 355 357				0 5344 2845 0 0 195 0 0 0 337 0 0 1302 0 1302	0 0 0 0 0 0 0 0 0 0	114 0 0 0 162 197 0 114 35 28 5 0 0	0 0 0 0 0 0 0 3i 0 26 0 0	6001 2570 7558 28180 1858 18822 5482 3241 3061 3236 6032 4071	0 0 0 2223 1\$570 0 1275 437 0 0 0 588 0	200 0 0 0 313 9 0 0 0 0 0 0	0 0 0 3008 37531 996 0 0 0 0 0 104 0 0	0 18131 775 17069 7453 1109 4385 48948 2708 12179 248 12650 2202 26749 2901
Ne 578T HT213 HT228 HT228 HT139 HT155 HT155 HT150 HT1778 HT1778 HT178 HT178 HT178 HT178 HT178 HT178			52 54 55 56 50 60 62 63 63 64 65 65	353 355 357				0 5344 2845 0 0 0 195 0 0 337 0 0 1302 0 1835	0 0 0 0 0 0 0 0 0 0 0	114 0 0 0 162 197 0 114 35 28 5 0 0	0 0 0 0 0 0 0 31 0 0 0 0 0 0 0 0 0 0 0 0	9001 2570 7556 28180 1858 18822 5462 3241 3061 3235 6032 4071 3571 5024 8175 4946	0 0 0 2225 1\$570 0 1275 437 0 0 0 588 0 0 121 121 0	200 0 0 0 313 0 37 0 0 0 0 94	0   0   0   0   0   0   0   0   0   0	0 18131 775 17059 7453 4109 4385 48948 2708 12179 248 12550 2202 26749 2901 1773 2724
No 578T HTZ13 HTZ28 HTT155 HTT155 HTT155 HTT10 HTT10 HTT10 HTT18 HTT18 HTT18 HTT18 HTT18 HTT18 HTT19 HTT19			52 54 56 56 50 60 62 63 64 65 65 66 67	353 355 357				0 \$344 2945 0 0 0 195 0 0 0 0 1302 0 1815 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	114 0 0 0 152 197 0 114 335 229 5 0 0 0 73	0 0 0 0 0 0 0 31 0 26 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	9001 2570 7556 26180 1858 18822 5462 3241 3061 3238 6032 4071 3571 5024 5175	0 0 0 2223 15570 0 1275 437 0 0 0 588 0 0 121 121 0 0 0 2 127 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	200 0 0 0 313 37 0 0 0 0 94 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 18131 775 17069 7453 1109 4385 48948 2708 12179 248 12650 2202 26749 2901 1773 2924 1369
Ne 578T HT213 HT228 HT228 HT139 HT155 HT155 HT150 HT1778 HT1778 HT178 HT178 HT178 HT178 HT178 HT178			52 54 55 56 50 60 62 63 64 64 65 65 66 67 69	353 355 357				0 \$344 2845 0 0 0 1956 0 0 3377 0 1302 0 1635 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	114 0 0 0 152 197 0 114 35 28 5 0 0 0 73	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	9001 2570 7550 26180 1858 18522 5482 3241 3061 3238 4071 5032 4071 5032 6175 6175 6184 894 4352	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	200 0 0 0 0 0 0 37 0 0 0 0 0 0 0 0 0 0 0	0 0 0 306 37531 986 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 18131 775 17069 7455 1109 4385 48948 2708 12179 248 12850 2202 28749 2991 1773 1389 3940
Ne 578T HT721 HT728 HT728 HT728 HT739 HT735 HT735 HT735 HT735 HT737 HT738 HT737 HT738 HT738 HT738 HT738 HT738 HT738 HT738 HT738 HT738 HT738 HT738 HT738 HT738 HT738 HT738 HT739 HT73			52 54 55 55 50 60 62 63 64 65 65 66 67 68 69 71	353 355 357				0 \$344 2945 0 0 0 195 0 0 0 0 1302 0 1815 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	114 0 0 162 197 0 114 35 28 0 0 0 28 0 6 1	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	9001 2570 7559 28180 1856 18322 5482 3241 3061 3238 6032 4971 3571 5024 8175 6946 894	0 0 0 2223 15570 0 1275 437 0 0 0 558 0 0 121 121 0 0	200 0 0 0 0 1 37 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0   0   0   0   0   0   0   0   0   0	0 18131 775 17069 7453 1109 4385 2708 2708 12709 248 12709 28719 28719 2772 28749 2901 1773 2924 1389 3940 986
ive 578T HTZ213 HTZ28 HTZ28 HTZ35 HTZ35 HTZ35 HTZ35 HTZ37 HT			52 54 55 55 50 60 62 63 64 65 65 66 67 68 69 70 71	353 355 357				0 5344 2845 0 0 195 0 0 0 337 0 0 1902 0 0 0 1835 0 0 0 1835 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	114 0 0 0 1552 197 0 114 35 229 5 0 0 0 273 0 28 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	6001 2870 7830 28180 1856 18822 2241 3061 2233 6032 4071 3571 5072 4071 4071 4071 4071 4071 4071 4071 4071	0   0   0   0   0   0   0   0   0   0	200 0 0 0 0 0 0 0 0 0 0 0 0	0   0   0   0   0   0   0   0   0   0	0 18131 775 17069 14535 1109 4355 2708 12179 248 12202 26749 2901 1771 2924 1369 3940 996 4445 3685 4721
Ne 578T  KT210  KT226  KT226  KT120			52 54 55 55 50 60 62 63 64 65 65 66 67 68 69 71	353 355 357				0 2945 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	114 0 0 0 162 197 197 114 325 5 5 0 0 0 0 0 0 0 0 114 325 325 325 325 325 325 325 325 325 325	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	6001 2870 7556 28100 1856 1852 2841 3051 3051 3051 3051 3051 3051 3051 305	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	200 0 0 0 313 32 37 77 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 3008 37531 0 0 429 0 0 0 0 104 0 0 0 104 0 0 0 0 0 0 0 0 0	0 18131 775 17063 77453 1109 4385 4584 2709 248 12179 248 12550 2202 26749 2901 17773 2924 1389 3986 4415 3685 4721 4721 5156 5156
ive 574T HTZ213 HTZ245 HTZ245 HTZ245 HTZ245 HTZ245 HTZ245 HTZ25 HTZ25 HTZ25 HTZ27 HT			52 54 55 56 50 60 62 63 64 65 65 66 69 70 71 72 73 74	353 355 357				0 5344 2845 0 0 195 0 0 0 0 1337 1302 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	114 0 0 0 1552 197 0 114 35 229 5 0 0 0 273 0 28 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	6001 77599 77599 18100 1856 1822 2241 2667 2023 4071 3071 4096 4096 4096 4096 4096 4096 4096 4096	0   0   0   0   0   0   0   0   0   0	200 0 0 0 313 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0   0   0   0   0   0   0   0   0   0	0 18131 775 17063 7453 1109 4385 48948 2708 12179 248 12650 26749 2901 1773 2924 13659 3940 9445 3685 4445 3685 4721 6154
Ne 578T  KT210  KT226  KT226  KT120			52 54 55 56 50 60 62 83 84 65 65 67 68 69 70 71 72 72 73 74 76	353 355 357				0 5344 2845 0 0 0 0 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	114 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	6001 77599 77599 18100 1856 18525 2241 2067 2235 4071 5024 4071 5024 4046 8944 4352 3324 4200 8945 4026 8945 4036 8945 4036 8945 4036 8945 4036 8945 4036 8945 8945 8945 8945 8945 8945 8945 8945	0   0   0   0   0   0   0   0   0   0	200 0 0 0 313 32 37 77 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 18131 775 17063 77453 1109 4385 4584 2709 248 12179 248 12550 2202 26749 2901 17773 2924 1389 3986 4415 3685 4721 4721 5156 5156
Ne 578T HT(21) HT(28) HT(28) HT(28) HT(18) H			\$2 \$4 \$5 \$5 \$5 \$5 \$5 \$6 \$6 \$6 \$6 \$6 \$6 \$6 \$7 \$9 \$9 \$7 \$7 \$7 \$7 \$7 \$7 \$7 \$7 \$7 \$7 \$7 \$7 \$7	353 355 357				0 5344 2845 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	114 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	9 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	6001 2570 7559 28190 1859 1852 5492 241 3061 323 6032 6032 5071 5071 604 603 603 603 603 603 603 603 603	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	200 0 0 0 1313 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 18131 775 17059 17059 17453 11025 45856 45856 45856 4586 27002 26749 2861 12773 2901 1771 1859 3865 4727 6155 5832 20222 2222 2222 2222 2222 2222 2222
Ne 578T  MT213  MT226  MT226  MT126  MT127  MT127  MT127  MT127  MT127  MT128  MT128  MT128  MT128  MT128  MT128  MT128  MT129  MT129  MT129  MT129  MT120  MT127  MT120  MT127  MT120  MT127			\$2 \$4 \$5 \$5 \$5 \$5 \$5 \$6 \$6 \$6 \$6 \$6 \$6 \$6 \$7 \$9 \$9 \$7 \$7 \$7 \$7 \$7 \$7 \$7 \$7 \$7 \$7 \$7 \$7 \$7	353 355 357				0 5344 545 543 545 543 555 560 0 0 0	000000000000000000000000000000000000000	114 0 0 0 0 0 0 1622 1927 0 0 1044 235 5 0 0 0 0 0 0 0 0 0 0 0 0 0 0	9 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	6001 2570 7354 28180 1856 1852 5482 2411 2061 2323 6032 4071 1572 4071 1572 4071 4071 4071 4071 4071 4071 4071 4071	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	200   200   313   30   313   30   313   30   313   30   315	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 18131 775 17059 17059 17453 11025 45856 45856 45856 4586 27002 26749 248 12650 2901 1773 2904 1905 4445 4585 4585 4727 2922 2924 1359 3665 4727 25020 2720 27212 27212 2720
Ne 578T  KT213  KT226  KT226  KT226  KT326  KT327  KT327  KT32  KT327  K			52 54 55 55 56 50 60 61 65 66 67 70 71 72 73 74 76 60 60 60 60 60 60 70 71 72 73 74 76 60 60 60 60 60 60 60 60 60 6	353 355 357				0 5344 2845 2845 2845 2845 2845 2845 2845 28	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	114 0 0 0 0 162 197 0 0 104 335 288 0 0 0 0 0 0 0 0 0 0 0 0 0 0 107 107 108 108 108 108 108 108 108 108	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	6001 2570 7559 28100 1850 18522 5462 2241 3061 3226 6032 4071 3271 5074 894 4452 440 541 452 440 541 452 440 451 452 440 451 451 451 451 451 451 451 451 451 451	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	200   0   0   0   0   0   0   0   0   0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 18131 7775 17059
Ne 578T  HT230  HT238  HT238  HT139  HT155  HT155  HT150  HT151  HT151  HT152  HT153  HT158  HT178  HT158  HT178  HT159			52 54 55 55 55 60 60 60 60 60 60 60 60 60 60 60 60 60	353 355 357				0 2945 2945 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	114 0 0 0 0 162 197 0 114 335 5 5 0 0 0 0 228 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	6001 2570 7354 28180 1856 1852 5482 2411 2061 2323 6032 4071 1572 4071 1572 4071 4071 4071 4071 4071 4071 4071 4071	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	200   200   313   30   313   30   313   30   313   30   315	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 18131 775 1705 976 1815 1816 1816 1816 1816 1816 1816 181
ive 578T INT213 INT238 INT288 INT388 INT381 INT3881   INT38881 INT388881  INT3888881 INT3888881 INT3888881 INT3888881 INT3888881 INT3888881 INT38888881 INT38888881 INT38888881 INT388888881 INT388888881 INT3888888881 INT38888888881 INT38888888881 INT			52 54 55 56 56 60 60 60 60 60 60 60 60 70 70 71 71 72 73 74 75 60 60 60 60 60 60 60 60 60 60	353 355 357				0 5344 220 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	114 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	6001 2670 77550 1850	0   0   0   0   0   0   0   0   0   0	200   0   0   0   0   0   0   0   0   0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 18131 775 1705 975 1202 1202 1202 1202 1202 1202 1202 120
Ne 578T  MT213  MT228  MT228  MT129			52 54 55 56 50 60 60 60 60 60 60 60 70 70 71 71 72 60 60 60 60 60 60 60 60 60 60	353 355 357				0 2945 2945 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	114 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	6001 2670 77550 78180 18550 18550 18522 5492 5293 5	0   0   0   0   0   0   0   0   0   0	200   0   0   0   0   0   0   0   0   0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 18131 7775 775 7755 7775 7775 7775 7775 77
ive 578T INT213 INT238 INT288 INT388 INT381 INT3881   INT38881 INT388881  INT3888881 INT3888881 INT3888881 INT3888881 INT3888881 INT3888881 INT38888881 INT38888881 INT38888881 INT388888881 INT388888881 INT3888888881 INT38888888881 INT38888888881 INT			\$2 \$4 \$5 \$5 \$5 \$6 \$6 \$6 \$6 \$6 \$6 \$6 \$6 \$6 \$7 \$9 \$9 \$9 \$7 \$7 \$7 \$7 \$7 \$7 \$7 \$7 \$7 \$7 \$7 \$7 \$7	353 355 357				0 5944 5 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6		114 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	6001 2570 7759, 781919 1002 100	0   0   0   0   0   0   0   0   0   0	200   0   0   0   0   0   0   0   0   0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 18/131 7753 17069 7453 11099 43689 2709 43689 2709 2709 2709 2709 2709 2709 2709 270
Ne 578T  MT213  MT226  MT226  MT226  MT127  MT127  MT127  MT127  MT128  MT128  MT128  MT128  MT128  MT128  MT129  MT129  MT127  MT129  MT127  MT129			\$2 \$52 \$55 \$55 \$55 \$55 \$55 \$55 \$55 \$55 \$	353 355 357				0 5944 20 10 10 10 10 10 10 10 10 10 10 10 10 10	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	114 0 0 0 0 0 0 0 152 152 152 153 23 23 23 23 23 27 27 27 27 27 27 27 27 27 27 27 27 27	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	6001 2570 7536 7536 7536 7536 7536 7536 7536 7536	0   0   0   0   0   0   0   0   0   0	200   0   0   0   0   0   0   0   0   0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 18131 775 17069 7453 11099 4385 48846 27090 12179 28749 28749 28749 28749 3840 996 4445 3685 4445 2725 6152 5932 2721 6152 5932 5932 5932 5932 6152 6152 6152 6152 6152 6152 6152 615
Ne 578T  MT213  MT228  MT228  MT129  MT229			\$2	353 355 357				0 5944 505 605 605 605 605 605 605 605 605 605	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	114 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	6001 2570 77549 77549 781919 7829 7829 7829 7829 7829 7829 7829 782	0   0   0   0   0   0   0   0   0   0	200   0   0   0   0   0   0   0   0   0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 18 131 7773 17963 11963 11963 11963 11963 12079 12179 248 248 2202 27749 2503 2503 2503 2503 2503 2503 2503 2503
ive 578T  INT213  INT228  INT288  INT38  INT			\$2 \$52 \$55 \$55 \$55 \$55 \$55 \$55 \$55 \$55 \$	353 355 357				0 5944 5945 694 694 694 694 694 694 694 694 694 694	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	114 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	6001 2570 7750 2570 7750 1550 1550 1550 1550 1550 1550 1	0   0   0   0   1   2   2   2   2   2   2   2   2   2	200   0   0   0   0   0   0   0   0   0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 18131 7773 17808 17808 17808 14809 14809 14809 14809 14809 14809 14809 14809 15809
Ne 578T  MT213  MT226  MT226  MT126  MT127  MT129  MT229			\$2	353 355 357				0 2945 2945 0 1956 1967 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	114 0 0 0 0 0 0 0 159 159 159 159 159 159 159 159 159 159	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	6001 2570 7730 781010 78100 781010 781010 781010 781010 781010 781010 781010 78101	0   0   0   0   0   0   0   0   0   0	200   0   0   0   0   0   0   0   0   0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 1011111111111111111111111111111111
New SYST  MT210  MT226  MT226  MT126  MT127  MT127  MT127  MT127  MT127  MT128  MT129  MT227			\$2	353 355 357				0 5944 50 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6		114   114   115	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	6001 2670 7836 78100 781	0   0   0   0   0   0   0   0   0   0	200   0   0   0   0   0   0   0   0   0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 1 11 11 11 11 11 11 11 11 11 11 11 1
Ne 5781  NT 205  NT 20			\$2	353 355 357				0 5944 594 594 594 594 594 695		114 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	6001 2570 7754 2570 7754 7754 7754 7754 7754 7754 7754 7	0   0   0   0   0   0   0   0   0   0	200   0   0   0   0   0   0   0   0   0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 19131 1913
Ne 9745  Ne 9745  NET 201  NET 205  NET			\$2	353 355 357				0 5944 5 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6		114   114   115	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	6001 2670 7836 78100 781	0   0   0   1275   1275   11773   0   11775	200   0   0   0   0   0   0   0   0   0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 1911 1911 1911 1911 1911 1911 1911
New SYST  MY 201  MY 2			\$2	353 355 357				0 2945 2945 0 195 195 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	114 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	6001 2670 77556 2670 77556 10557 2610 10557 2610 10557 2610 2611 2611 2611 2611 2611 2611 2611	0   0   0   0   0   0   0   0   0   0	200   0   0   0   0   0   0   0   0   0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 1911 1911 1911 1911 1911 1911 1911
Ne 9745  Ne 9745  Ne 1745  NET 255  NET			\$2	353 355 357				0		114 0 0 0 0 0 0 0 152 162 162 162 163 164 154 154 164 164 165 165 166 166 166 166 166 166 166 166	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	6001 2670 77546 77540 77540 781818 78	0   0   0   0   0   0   0   0   0   0	200   200   313	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 19131 19
New SYST  MY 201  MY 2			\$2	353 355 357				0 2945 2945 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	114   0   0   0   0   0   0   0   0   0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	6001 2670 77540 77	0   0   0   0   0   0   0   0   0   0	200   0   0   0   0   0   0   0   0   0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 19131 19
ive 578T  INT 211  INT 228  INT 228  INT 238  INT 238  INT 238  INT 237  INT 237  INT 237  INT 247  IN			\$2	353 355 357				0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	114 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	6001 2570 7754 2570 7754 7754 7754 7754 7754 7754 7754 7	0   0   0   0   0   0   0   0   0   0	200   0   0   0   0   0   0   0   0   0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 19131 19
Ne 578T  KT215  KT215  KT226  KT226  KT126  KT127  KT129  KT129  KT1129  KT129		\$2	353 355 357				0 5044 2 5045 5046 504 504 504 504 504 504 504 504 504 504	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	114   0   0   0   0   0   0   0   0   0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	6001 2670 77540 77	0   0   0   0   1275	200   0   0   0   0   0   0   0   0   0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 19131 19	
ive 5785 INT213 INT213 INT228 INT288 INT38	JG 181		\$2	353 355 357				0 2945 2945 0 195 0 196 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	114 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	6001 2670 77549 77549 781919 7819 78	0   0   0   1270   1271	200   0   0   0   0   0   0   0   0   0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 19131 19
Ne 578T  MT213  MT226  MT226  MT127  MT128  MT129  MT29  MT	ISQ 181 192 193 193 193 193 193 193 193 193 193 193		\$2	353 355 357				0 5044 2 5045 5046 504 504 504 504 504 504 504 504 504 504	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	114 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	6001 2570 77546 77546 77546 781092 78	0   0   0   0   0   0   0   0   0   0	200   0   0   0   0   0   0   0   0   0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 19131 1913

175 Table 3 (cont'd)

Tissue	Tumor-sym	Normal-sym	Tumor - 1a	Yumor celta	Normal	Endos	p53	SEQ 044 1	RSEQ 45 A	A SEQ 47 A	A SEC 44 A	SEQ 49 A	ASEQ_51 K	ASEQ 32 A	NSEO 54 C	CSEQ 35 CL
He STRT MCF-T/ADR-RES	153							4159	1	0 6	1	4775	5!	01 67	0 153	15 18395
MCF7	151	<del> </del>		<del></del>	<del> </del>	<del> </del>	-	303		0 16	) 183		2	0; 11 0) 160		7 4938 0 27225
M14	149									0 150	)[	388	168	1 50	<del>2</del> 1	0 5925
UACC-257 UACC-62	147	<del> </del> -	<del> </del> -	<del></del>		├				0 4		533	5! 59	6;	0 91	3 14636
SK-MEL-26	144							894		0 10		4298	19		125	6 6386
UO-31 SK-MEL-5	143	<del> </del>	<del> </del>			<b>├</b> ──	<del> </del>	755		0 1		5134	1 161		6 191	0 5096 3 6211
KM-12	141							1090		0	2	2880	29	9 43	7 86	5 1796
SK-MEL-2 HCT-15	139	<del> </del>	+	-	-	<del> </del>		- 6		0 0		398	39	9 17		
Matrie-3M	138	<u> </u>						1858		0) (	)(	494	r! . 2	5 31		
LOX MAVI	137	1			-			2152 6439	<b> </b>	0 22	333	5549	!	0	0	0! 5235
SW-620	135		1					1038		0] 37		3684	118	7 38	4 65	9 2486
TK-10 HCT 116	134		F	ļ		-		1665		0 0	10	3620	166	3 34	4 99	5 11184
786-0	132							515 2701	<del> </del>	0 10	104	3803	106	5 19 0 37	37	0 4667 4 8085
HCC-2998 ACHN	130							1371		0](	) (	6532	76	7 26	1 77	0 2945
PC-3	129		<del></del>				<u> </u>	- 8	<del></del>		104	4590		7 10	2 99 D 24	
RXF 393 DU-145	128					=		3345	1	0 11	212	3357		36	96	2 19597
Cak-1	126		<del> </del>					455		0 132	160	2437 492	73	9 26		7 7704
SR A496	125		F					1045		0 2		3576	<u>u                                     </u>	0	52	9 7915
RPMI 8226	123	1	<del> </del>			<u> </u>		2368		0 126		3952		73:	21 401	1 12101 7 5650
SN12C HL-60	122	-					-	- 8		0 0		4346	176	350	114	61 10454
MOLT-4	120		t			<u> </u>		591		0 24			55	20	3 328	0 7486 3 4657
OVCAR-5 K-562	119	ļ						575		0 56	30	4525		0 6:	5 436	5 7866
OVCAR-4	117							1705				8408	235	37.	2 210	2 12924
CCRF-CEM OVCAR-3	116		<b></b>				=	518 2335		0 70	i	3941	16	181	85.	2 14584
SF-539	114							Z335		0 56		3837	91	180	28	1 5529 3 4097
HOP-62 SF-295	113		-					527		0	188	3830	20	2	91	1 14232
A549/ATCC	111_				=		ᆮ	678 1174		9 9	210	8431	177	5 39°		8 10018 9 11839
SF-268 NCI-HS22	110		-			$\vdash$		863		0	112	2981	43	10.	189	3 5908
U251	108							1687		9 21	474				121	
NCI-H460 SNB-75	107	ļ <del></del>					_	294 683		221		4589	65	345	<u> </u>	6 5432
NCI-H322M	105							683		76						0 1015
SNB-19 NCI-H226	104					$\vdash$		20 4486		0 63 0 19	- 0	3171				8 4580
5K-OV-3	102							942		59	0	3732			1	0 11044
NCI-H23 IGROV1	100							200		142						
EKVX	96							793		14	167	3052	1	1. 445		8 6847
OVCAR-8 HOP-82	98									72				40		
h Sproblests 3/31/92 #12	45							1168	1 (	123		3977	163	85	133	8 2848
h adult SMC 10/21/92 #17 h keratnocytes 2/25/92 #10	46							2238 1043	- 9	112		4154		96	747	21 4832
TCGP	26							0		115	326	3112 3362		276	311570	
A549 - 1 A549 - 3							¥	497 317		37					H	0) 0
A549 - 4							wī	0	26	153				)		
A549 - 5 A549 - 7	<del> </del> -						wf	321	109	62	0	8				0 0
EKVX - 1							mulant	5861	2130	285		0	<u> </u>	1!		0
BOX-3		<del></del>	-				mutant	2147 2865			0					0 0
EKVX - 5							mutani	1030		0				1 0	)	0 • 0
EKVX - 7 MCF-7 - 1		<del></del>					mutani wi	8				0	<del> </del>			0 0
MCF-7 - 3 MCF-7 - 4							wt	403			0	0				0 10
MCF-7 - 5							wt .	750 3124								0 0
MCF-7 - 7 ADR-RES - 1							wt_ mutant	849								0
ADR-RES - 3							mutent	30924				- 6				0 0
ADR-RES - 4 ADR-RES - 5							mutani mutani	4757 835								0
ADR-RES - 7							muture.	748	361	11	0	0				0,
WI 38 - 1 WI 38 - 3							w1	2518 1849								0 0
WI 38 - 4							wi	0		0						6
WI 38 - 5 WI 38 - 7	<b></b>	<b></b>	<del> </del>				wi	3098 812		37				0 0		0 0
HeLe - 1							HPV E6		395	7	0	0	1. 6			0
HeLe - 3 HeLe - 4	<del></del>		<del> </del>				HPV E6	852 848								0 0
Hala-5							HPV E6	2647	766	172	0	0				0 0
Hei.e - 7 H1299 - 1							MPV E6	429	550							0 0
H1299 - 3					$\Box$		mertant	1149		193	0				1	0
H1299 - 4 H1299 - 5			<del></del>				muteri muteri	1155 819	63							0 0
H1299 - 7					=		mutent	0	0	71	. 0	. 0				0
A549 - 2 EXVX - 2							enutent	751 21741								
HCT-116 - 1							wt	649	0	206		0				0
HCT-116 - 2 HT29 - 2							wt muterii	9208 407								0 0
SF539 - 1 SF539 - 2					==		*	1107	261	O O	0	0				0
SF-268-1							wt mutum)	523 9794	202	139						9
SF-268-2 OVCAR-4 - 1					=		mutant wt	11614	4311	265		0				0
OVCAR-4 - 2							\$	2660 0	٥	0	0	0			1 0	0
OVCAR-5 - 1 OVCAR-5 - 2							mutant	705	0	0	0	0				0
MCF-7 - 2							wt.	367 2194	0	43						
ADR-RES - 2							MPV 66	410 2741	747	86		0				)! 0
HeLa - 2 SW480 - 1						- 1	ENAME:	883	1075	209	0	. 0		0		0
SW480 - 2							mutan)	613	718	50	0	0			·	0
H1299 - 2 C33A - 1							mutani mutani	322 318	571 0			0	0			
C33A - 2							mutant	6480	0	75	. 0	0	0	0	1 0	). 0
U2OS - 1 U2OS - 2							meteri meteri	8301 3542	1266			0		0		
Hu68 - 1 Hu68 - 2					-		m. m	2216 4302	164 734	45	0	0				0
WI 38 - 2							M	0	631	21		0	. 0	0		
Mildrell - 1 Mildrell - 2				<del>T</del>			-7	513 310	0		9		0			
Mikhali - 3								50334	0	0	0	0	•			
Mildhad - 4 Mildhad - 5				T	<del></del> -			54762 5016	908		0		0			0
Machael - 6								9098	738	311	0					): 0
Maknad - 8 Mikhad - 9				-		=		2854 2068	0	37	0	D		1 0	. 0	0
								4V00			. 0					0

176 Table 3 (contd)

Tinava	Turnor-ave	Normal-sym	Yumar - 1-	Tugan and	10	The state of	Inte	ISPO **	AIREA 1	des A	Nec-1	lade :	-les:		
Cant				166	-ima	C. P4008	1943	SEQ 36 A	A SEQ 57 W	15EQ 60 A	7! 1028	SEQ 66 C	A SEC 68 HE		SEQ 73 HR SEQ 78 A
766-0 T-47D	+			168	$\blacksquare$	+	_	53:	3 952	6 22	7 976	272	8859	5204	82251 55570
X=-3				171	1	$\pm$	<del> </del>	560	5 8511 0 193	3	0 1074 0 234				19722 3993
CRL 1441 RNA B/30 7817 untrested • DNese				181		=		270	310	•	0 24				
KB poly A+			<del> </del>	194	+	<del></del>	+	19		0	0 108	1 0			230 14562
MQS paly A+	+		$\vdash$	196				29	7 326	51 827	7] 0		526		
UACC-62				198	<del> </del>	<del> </del>	+	149,			358				14597 2614
MCF-7/ADR-RES UTOS (Mundy) poly a+				202				185	2221	75	5 D		381	1444	2582 14607
WISH (Collegen) poly A+			<del>                                     </del>	206	+	+	+	150			104			1028 579	617 9607
458 medulio mRNA CCL137 RNA 3/21/88	+			208					18176	3	623	53	0	2362	725 11442 2915 60563
WI-38 72h 0.5%FBS, 24h 10% FBS			<u> </u>	219	_	-	+	219	1068	1196	298	34		1447	915: 23844 0 41474
CRL 1441 + TPA (24h) 8/30 Ken-1	+			220			_		5587		31	693	0	1065	63 18180
Ken-2				221		=	+	2280 705	2513		1 115				158 45268 41 41277
Ken-4 HOP-92	<del> </del>	<del>                                     </del>		225		-	-	521	4040				1303	22421	89 30345
MOLT-4				242	1		+	646	8364					17731 3182	13338 19084 39419 23972
EKVX HL-60	+	<del> </del>	ļ	243		-		6	13083		326		3139	6452	109714 30253
NCI-HZ)				245		$\vdash$		950	13057					3689 5364	15999 39367 95596; 46201
ASIGNATIC	<del></del>		<del></del>	246	┼	<del> </del>	├	69					354	2272	18378 26669
SR OVČAR-3				248			$\perp$	0	1814	383			691 244	1991 2897	2385 18971 10201 17287
HCT-15	<del> </del>		-	249 250	<del> </del>	<del> </del>	┼-	- 8				120	1028	2424	7704 20678
OVCAR-4				251				223	314			189		4642 905	105630 27562 1481 7613
UQ-31 OVCAR-S	+	<del> </del>	<del> </del>	252 253	+		<del> </del>	372 2585	3404 9438			- 6 57	143	547	1109 6300
SN12C				254					5112			108		3348 2875	12208 24504 26805: 16317
LOX MAYI		<u> </u>		255 256	+	<del> </del>	<del>-</del>	823				0	1122	1359	356331 14140
IGROV1 SK-MEL-2	$\vdash$			257	$\overline{}$			1194	8352	758	716	61 86	2032	5283 3644	30147 38548 28934 31704
SK-OV-3				258 259	<del>!                                    </del>	<del> </del>	+	65				0	0	953	4982 15816
SK-MEL-5 SF-539	+	<u> </u>		260	<u> </u>			135	3911	ō	48	103	1340	3782 1148	8318 17004 3811 13582
SK-ME1-28				261 262	<del></del>	<u> </u>	<u> </u>	3932	7037	0		150	7673 1713	5550 1591	62279 51506
K-562 UACC-257	+			263	-			987	8200	1949	1685	99	9059	4576	195694 61730
M14				264 265				0	2639	0		214	1590	2366 916	3496 29095 1176 17725
MCF7 MDA-MB-435	<del> </del>			267 269	$\vdash =$			829	16845	920	955	604	4698	6019	79777 80630
HT279				270			_	14	6376 4493			0		1657 2525	1148 24187 281 41491
MDA-N Y78 poly A+	<del> </del>		-	271	$\vdash$		$\vdash$	276 0		0	354	92	1299	1838	5866 18906
KHQS poly A+				289				٥	20758	17445		238	3785 6785	6025 4275	24954 77961 36066 76961
HTB36 24h YPA RNA 6/23 HELA-EXP-031890	<del> </del>			300		_	-	783 634	3981			. 0	2296	2492	221 31917
HTB36 Oh RNA HT347				322				1461	24454	- 0		989	1590 3512	2848 6180	4161 39714 3044 91684
456 medulis RIVA				323	<del>                                     </del>			404 1327	4566 40573	0	0	0 748	2939	3484 4386	15822 40401
NCI-HZ26 HOP-62				336				672	6101	721		0	1515	2111	476 69088 2329 37119
MDA-MB-231				337	<u> </u>			1105			906 9728	78 1217	25352	1717	36496 21036
U251 PT cells poly A+	<del> </del>		I	339				132	90374	1171	18256	3821	76758	33690	259035 103178 2025349 111922
PC-3 HCC-2996				341				483 177		62	362	2330	1987	2005	45862 16256 40554 71885
SW-620	<del>                                     </del>			343				92	8206	0	552	569	1782	2289	23873 21576
HT192				346				1001	7776 7290	408	621 182	200	1251	2046 S254	10731 24715 2082 65825
COLO 205 HT218	<del>  </del>			347				162	9047 4819	0	306	0	0	689	1304 8915
KM-12 HT151				349				49	11052	- 8	77 406	158	691	1385	391 36949 34049 17488
A498				350 351	<del>                                     </del>			138	5054 j 20305 i	- 0	- 61	0.	723	3737	497 45600
HT393 RXF 393	$\vdash$			352				726	15335	57	0	1564	1038 2602	2626 4435	4743: 30375 5637 60953
TK-10				353 355			-	738	78666	694	3780	73 1673	348 23028	12524	7239 24306 129790 71952
Melme-3M He 578T			=	357 359				2111	93276	13897	36286	2444	554791	34972	201421 150800
HT213			50	339					9184 5740	47		82	2391 978	2875) 1700	6581 46992 28 57671
HT288 HT139	<del></del> i		52					179	8067	D	0	272	783	2581	75411 84143
HT155			56					921	52431 66901	_ 0	281	635 632	2394	1926 2131	276 65037 2121 61017
HT163 HT170	<del>                                     </del>		58				7	1082	1302	364	0	253	261	1598	540 81243
HT172 HT136			62					37	15971	- 8	252 i	17	1662 284	975	15427 83039 0 46245
HT178			64		$\vdash$			31	2623 3195	0	. 0	43	797	1070	4034 45891
HT 154			65					0	1277	0: 2364	- 0	145	108	974 1138	600 51853 0 52719
HT189		<del></del> 7	66 — 67					276 427	- 2597 4940	0	- 58	- e	862	685	197 43129
HT189 HT143		==	68					691	4088	288	122	229	269 346	455 1043	1239 26590 3366 78481
HT190			69 70					2067	245 5719	0 964	0 58	0	161	828	42 38405
HT 145 HT 227	$\vdash$		71	-				1053	3301	539	0	74	3282	1854	0 59909 230 58867
HT302			73					- 8	18129	0	93 439	163	2496	1925	2571 65548
HT314 HT317	-		74 76					. 0	10943	138	0	41	279	2601 1755	665 84661 1196 51097
Machinetorne #425 11/8			n		+		<del></del> +	275	25792	0	2002 126	651 250	98	5151 3011	5403 100931
HT323 HT327			78	==		=		0	7907	0	1120	58	335	3764	615 59514 1641 107547
17305			82					2241	7044	112	267	41 201	934 2495	1737 2254	688 52009 813 70437
HT146 HT348	<del></del>		85		-			2097 2368	790	545	142		- 0	598	961 12152
HT31)			170			一		1002	5054 3027	1312	389	203	3609 508	1570 3081	2273 49949 1158 57188
HT396 HT140	$\vdash$		185		<u></u>	$\dashv$	$\neg \exists$	2942	11424	603	258	0	- 01	1550	614 31322
4T281	$=$ = $\pm$		189			二	二寸	. 0	7338	- 8	317	70	484	1007 1916	0 19444 . 0 41150
-TT372 TCGP			191	<del></del>			<b>-</b>	195	2899 2446	- 8	130	104	0	1932	708 59962
17160 17307			216				=	_ 01	1990	1000	114	33	139 749	1578 937	0 18184
(T369	=		Z17 ZZ4	<del></del>		<del></del> F		- 0	3175 12133	- 0	0	210	1003	1067	731 21628
(7370	-		226		$=\pm$			64	2565	0	125	177	1017	2374 1556	01 27470
man man		<del></del>	226 230			$-\Box$		967	490Z	01		0i	1523	2322	1349 34533
(1382 Brusbiessone RNA			236		=	$= \pm$	$=\pm$	1161	5719	518	56	0	3205	2839	443 25963 1024 43216
T334		<del></del>	281 299		-			- 0	10149/ 20076	0 ! D:	0!	295	155	693	0 5493
1738 17382			30:			=		139	13101	313	650	- 0	5897 899	5479 2548	14342 67794 2090 34982
(T394			315	<del></del> -T		<del></del> -F		1373	4032 5204	0	0	48	1315	1461	6518 30163
T312			219			ightharpoonup		270	3948	189	248 . 5567	21	1008 560	2695.	01 35234
(T162	<del></del>		325 35e		$ \top$		$ \mp$	357 553	2017. 5137:		306	01	0 i	1241	565 22972
T157			360						19069	0:	21:	0:	1105	4933	3677 60581 1407 140477
470 IDA-N	161			<del></del>	-F	<del>-  </del>	$\neg \top$	3006 1387	307241 291691	5571	1575+	2021;	6944	1536	13760 45303
IDA-MB-435	156	<b>==</b> ==				=		847	17967	1029 3441	1361 2565	6882 5642	17212	1166	8784 i 35475 13089 33644
DA-MB-231	157		(_	7		7	- 1	570	50640	2818!	2748	17271	42195	2891	10358 68995

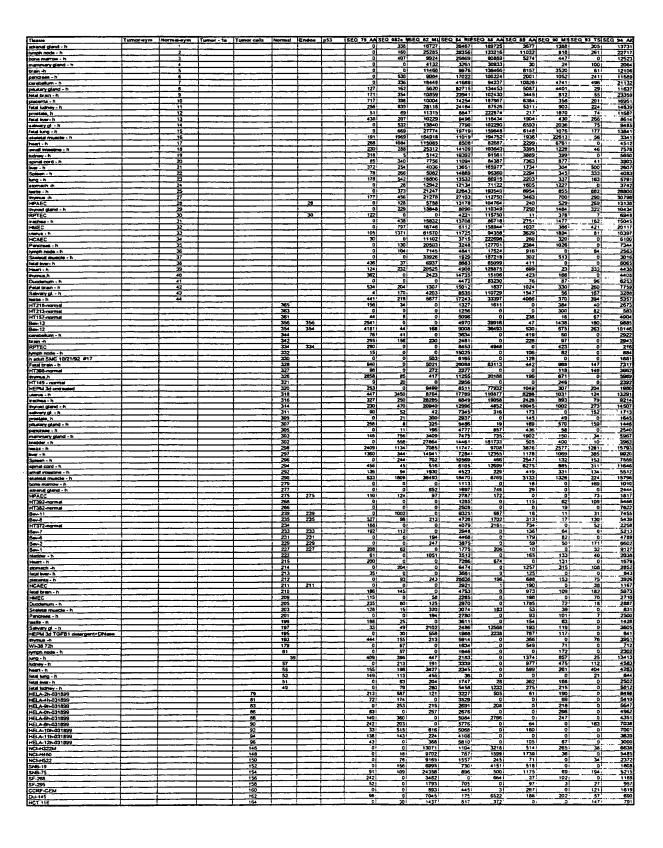
177 Table 3 (contd)

Thisue	Tumor-sym	Normal-sym	Tumor - 1a	Turnor calls	Normal	Fndos	In53	ISEO 56 A	SEO ST W	SEO 60 A	AISEO 63 ME	SEO 64 C4	4 E E O 2 A 100	4660 *** 0	SEQ 73_HR	SEO 18 A
He STAT	155								1 41445	51 64	7 1696	3442	20751		8395	55674
MCF-7/ADR-RES MCF7	153 151		-			-		225				488	22338	1868	39921	54013
MS4	149	<del>                                     </del>	<del>†</del>	<del> </del> -	├──	+	+	398					11886	3485	22510:	81756 69408
UACC-257	147							154			4 7208	163	8997	2195	17973	61725
LIACC-62 SK-MEL-28	145		<del> </del>	<del></del>	<del>                                     </del>	+	<del></del>	500			0 2146 6 577				4231 2990	41268 56931
UO-31	143						=	441				98	14005	2232	3934	105691
SK-MEL-5 KM-12	142	<del> </del>	<del> </del>	<del></del>		<b>⊹</b>	┼	118							9595   64	42911
SK-MEL-2	140							196	14486	5 322	1 795	1827	7349		7479	62671
HCT-15 Maine-3M	139 138	<del>                                     </del>	<del>                                     </del>	<del> </del>	├	├	<del> </del>	744 172	12275				4927	2667	7421	71198
COLO 205	137							248-	9160	279	51 439	1949	13401	2036	7321 2407	42597 98313
LOX MMI SW-620	136 135	<del> </del>	<b></b>			-	├	50:			2 3101 1 1807	4339	32433	892	8051	33734
TK-10	134			<u> </u>		$\pm$	-	54					10151	1195	2768 11381	38389 42220
HCT 116	133	-						1015				413	11794	2013	1498	39595
MCC-2998	131	1	f	t	<del> </del>	<del> </del>		1700						1670	7153 3255	41603 74996
ACHN	130					_		610			1253	645	21377	1466	7925	49258
PC-3 RXF 393	129 128	<del> </del>	<del> </del>		├	<del> </del>	┼	106					14268 20896		13035	45570 43831
DU-145	127							1200	9043	100	126	178	4962	2174	3958	46338
Calc-1 SR	126 125	<del> </del>	<del> </del>	<del> </del>	—	<b>├</b> ──	<b>├</b> ──	98					4696 1754	1933 2308	15823 4070	42979 44677
A498	124							931;	19949	35	295	0	14129	2475	10969	49897
RPMI 8226 SN12C	123 122	<del></del>	<del> </del>	<del> </del>	<del> </del>	₩	<del> </del>	1 8					580 6784	3030 2447	5708 106771	65175 75056
HL-60	121							393	4211	64				2057	2980	56854
MOLT-4 OVCAR-5	120 119	<del> </del>	<del> </del>			-	-	859				811	5501	13131	7213	70186
K-562	115							1044	4812	2234	360			969 1771	32826 9526	40584 56039
OVCAR-4 CCRF-CEM	117			<b></b>	<del></del>		<b>├</b> ─	2174					14315	1406	21344	44925
OVCAR-3	115							555	6682	236	1091	179			7736 25044	55652 42501
SF-539 HOP-62	114				-	$\vdash$	-	1112						1247	4955	41075
SF-295	112							200	7254	304	1051	2776	8751		24991 16984	25387 47319
A549/ATCC SF-268	111					-	-	1371	14738		3749	2445	18296	1303	66894	51944
NCHH5Z2	109							1333	10129	1948	3385	1263		1090 2094	15265	32506 42496
U251 NCL+4650	108	=				$\vdash$		1614	9600	2187	374	1611	29319	2229	10968	53640
SNB-75	106							1091	7303	127	539	25	20030	1506	32438 1580	40200 40399
NCI-H322M SNR. 19	105							3683	13987	3336	3512	473	11090	2166	20863	68,294
SN8-19 NCI-H226	103	=	$\sqsubseteq$		<del></del> -	<u> </u>		922		1415	598 2967	329 372	14989 7863	2894 4474	9129	52719 103492
SK-OV-3 NCI-HZ2	102						=		10957	671	740	482	5154	2758	8202	51778
IGROV1	100					<del> </del>	<del></del>	972 672	12935 10901	1798	5027 295	716 665	1791 3356	3129	7930	54491 55870
EKVX	99							1 0	9485	898	3388	217	4065	2078	31182	42470
OVCAR-8 HOP-92	95 97	<b></b>	ļ	ļ		├	_	347		2432	2897	574 792	5534 12382	1949 2385	4824 31301	49956 56630
in fibroblests 3/31/92 #12	48							1506	4900		3536	215	24750	1914	5365	92900
h adult SMC 10/21/92 #17 h termocytes 2/25/92 #10	45						├	4753					26767 16944	1464	10148 5161	75029
TCGP	26							509					\$A29	2429	9414	73876 61036
A549 - 1 A549 - 3							w	- 8		567		0	1876	331	14898	19283
A549 - 4							wf		3769					314 157	3847 11425	10191
A549 - 5 A549 - 7		<b></b>					wt	0				- 6	486	242	15448	13282
EKVX - 1							mutant	. 0	7918			0			12240 27454	20201 14020
EKVX - 4		<b>-</b>				<u> </u>	mutant	- 8				0	2883	1003	76154 7118	19451
EKVX - 5							meteri	0	2062	442				397 781	18082	16820 27269
EKVX - 7 MCF-7 - 1						_	muteni wi	0	5306 2465	1404		0		1385	5245	36616
MCF-7 - 3							*		4324			. 0		267 321	11222	15611
MCF-7 - 4 MCF-7 - 5						_	M	0	2671					191	16894	15090
MCF-7 - 7							wt	- 8	2515		341	0			24367 9134	14499
ADR-RES - 1							mutent	0	13125	0	4465	. 0		960	48482	43329
ADR-RES - 1 ADR-RES - 4					_		mutent	- 0	7895 3513					715 535	10664	15827 22994
ADR-RES - 5							muterd	0	1614	0	5674	0	572	116	18216	11995
AOR-RES - 7 WI 38 - 1							mutent wi	0	11054	Ö	1743	0			23088	17965 21030
Wt 38 - 3 Wt 38 - 4							<b>w</b> 1	1	9568	317	2832	. 0	2774	777	23796	13274
Wł 38 - 5							*	0	B553	. 0		0	2280 1877	795 750	25508 6930	14200
WI 38 - 7							¥	0	6181	461	897	0	966	1033	12862	13392
HeLa • 1 HeLa • 3						<u> </u>	HPV E6	0	2972 6135	1045		0	783 206	381	9680 19037	13265
Hat.a - 4							HPV E6	a	1902	787	1330	ol	263	619	11306	10796
HeLe - 5 HeLe - 7							HPV E6	0	8774 5057	348	2859 1004	0	2129 1673	634 660	16576	18512
H1299 - 1 H1299 - 3							mutant	0	5732	0	1826	. 0	488	769	13209	13626
H1299 - 4							mutent	0			3638	0	581 1997	547 567	4846 32306	12467 15925
H1299 - 5 H1299 - 7							muterit	- 0	3290		2060		1547	552:	9675	17547
A549 - 2							muterit	- 8				0	565 369	234 479	7747	13714
EKVX - 2 HCT-116 - 1							myteni wi			0	1255	0}	896	386	16174	16569
HCT-116 - 2							¥	8				0	1687 \$166	1682	13342 84458	61632 12601
HT29 - 2 SF539 - 1							mutant	0		696	2260	0	1581	581	28757	15526
SF539 - 2							wi wi	- 0				0	774	285	10468;	10847 14933
SF-268-1							mutent	0	11769	. 0	1105	0	3283	1120	16384	18521
SF-268-2 OVCAR-4 - 1							muterii wi	- 0	2968			9	2007 1685	1179 675	22525 9858	14395 24261
OVCAR-4 - 2							w	0	4382	688	3277		1872	583	230421	59463
OVCAR-5 - 1 OVCAR-5 - 2							mutani	- 8		350		0		269 278	12738 : 6986 :	11007
MCF-7 - 2							wt	0	2299	261	4687	0	630	122	7463	11768
ADR-RES - 2 HaLa - 2							MERENI MPV E6	- 8				0	814 i	654 B42	9941 40273	10902
SW480 - 1							mutani	4 0	6648	33	2511	0	1590	1162	44983	23143
SW480 - 2 H1299 - 2							mutani mutani	0	2850 7012	0			915 1502	538 864	28975 23857	19496 24461
C33A - 1					i		mutani	0	5679	0	0	0	570	230	473201	1,2514
C33A - 2 UZOS - 1					-		mutent '	0	3255 10292	604		0	978	208	8221	8913
U20S · 2							muteri	0	5298	749	9373	0	2116 3282	1959	52556 56322	31159 27447
He68 - 1 He68 - 2							*	0	7177 M34	447 403	1091	. 0	1155	415	11483	11664
WI 38 - 2							w	0	13625	489	1093	0	1883	746 732	9799 11794	17867 15250
Mikhail - 1 Mikhail - 2								0	8968	0	2718	0	1113	399	12501	14913
Methell - 3			+					- 0	12729			0	1618 686	386 466	13395	14118
Michael - 4						=	$\Box$	. 0	32682	0	0	- 0	1087	5491	4312	20874
Mikhai - 5 Mikhai - 6								0	13524	0	- 0	0	3366	1256	6031	11992 21144
								ò			5682			4350		23661
Methel - 8 Methel pi - 9		<del></del>			<del></del> +			- 0				01	3784 2077	1359	28629 4931	70644

178. Table 3 (contd)

Thous	I V	Normal-sym	Names de	IV.—— andla	internal	Endos	1041	SEO ME A	Jen er w	4 8 E O 40 A	VESO 61 NE	1660 64 C	SEO 64 HIS	40 114 614	EO 71 MOIS	10 11 44
DePeno-7	1,5	/	10	Trumber Comm	1	1			50728					1021	16539	11948
DaPeng-6									25361	1. 84	3297	9	2819	569	23676	14951
DePeng-S				<del> </del>		<b>├</b> ──	├	<del> </del>	26319					1086	52757 493051	12234
DaPang-11 DaPang-12	<del> </del>		<del></del>	<del> </del>		<del></del>		<del>                                     </del>				8		892	58983	11807
DaPang-10									18015		1366	0	4270	801	34062	11401
DePene 1		<del> </del>			<b>├</b>	<del>!</del>								10221 783	20201	22149
OsPeng-2 DsPeng-3		<del> </del>	<del></del>	<del> </del>	<del>                                     </del>	<del>                                     </del>		<del> i</del>					501:	9211	15252 31807	18156 25569
OsPerg-4									4899					680	20143	25155
DaPeng-5			<u> </u>					- 9				:0	1016.	340;	9931	12544
DePeng-6 A549 - 8		<del> </del>	<del>                                     </del>			-	w1						465 2260	398	1929	13833
EKVX - 8					1		Waster11		6749		5061	i i		903	74268	14160
HCT-116 - 7							~				89		812	478	84 13	12863
HCT-116 - 6 HT29 - 1				<del></del>	-		muteri	- 5					1494	391 d 451	11432 29516	18908 21737
HT29 - 7							materi	ľ	1053		54	0	307	209	91851	13162
HT29 - 6							mutent				2992	0		594	16207	19784
5F539 - 7 5F539 - 8	<del> </del>		<del></del>				<del>-</del>				966	0	1074 856	1066	12405	17988 16098
SF-268-7							mutent						1316	420	14248	15443
SF-268-8							makent.				1884	, o	2052	568	12101	14424
OVCAR-4 - 7 OVCAR-4 - 8			<del> </del>	-	<del> </del>	<del></del>	wt	<del> </del>					3077	730	3378 17308	14259 16946
OVCAR-S - 7							mutent				1750		19	1330	20088	37871
OVCAR-S - 8							multant			11046	46	0	2526	289	8074	10551
MCF-7 - 6 ADR-RES - 8							musent		4047				542 479	451 99	7975	15873 12562
Male - 8							HPV E6						1023	705	11463	19305
SW480 - 7							mutent	0	3941	559	846	0	1028	212	13765	11456
SW480 - 8 H1290 - 6	<del></del>	<del>-</del>	<del></del>	<del></del>	<del></del>		mutani mutani	0	3995		1133		987	459 460	19827 8507	10513
C33A · 7			<u> </u>						6455		131	0	934	331	1068	11745
C33A - 8							mutent		4384		456		1860	1422	9025	35099
U2OS - 7 U2OS - 8	<del></del>	<del></del>		<del></del>			muteril muteril		5463 4223		553 1921	0	1824 2486	251 614	21545 32498	18584
Ha68 - 7							¥	9	4235	17044	462	0	885	614	10895	18314
Hs68 - 8							w	9	4538		1101	0	573	583	3569	17704
WI 38 - 6 456 medullo RNA	<del></del>		<del> </del>	<del></del>	<del></del>	<del>                                     </del>	4	219			4637	322	11543	890 2288	7101 4332	12515
CRL1572 3/17/89				<u> </u>					1425	79	268		or-	1482	969	33047
Ber-4						84		1356	7179	1 0	471	66	4171	2041	13126	60734
HT368 HT378	<del></del>	<del> </del>	<del></del>	<del>                                     </del>	<del></del>	<del> </del>	<del> </del>	394			192	225	970	1504	451	51232 64598
HT385								2684	23776	1052	187	825	1605	3483	3271	115925
HT306								494						2614	74601	73383
Ber-5	<del></del>					173		142						2663 1943	2513	47794 27812
Bar-9						177								1821	763	37803
h har etmocytes 2/25/92 #10								_			0	878		1884	280	44367
HTB10						237	_	1100				31		2631 5317	16951	63544 84103
h fibrobleste 3/31/92 #12								165						2497	119	63251
prostate, h								97						1829	. 01	71260
MNNG-OS poly A+ SA-OS (Munoly) poly A+		<b></b>	<del> </del>	<del> </del>			$\vdash$	598				186		2510	3973	68936 62966
MK poly A+								272				1131		3944	51411	46333
HCT-116 - 3							<b>M</b>							457	6561	14135
HCT-116 - 4 HCT-116 - 5				<b> </b>			3	- 8						389	13553	16473
HCT-116 - 6							¥		5156	1378		ő		483	11650	12955
A549 - 6							7		777			0		315	2191	14864
HT29 - 3 EXVX - 6		-					muteri muteri	0	3211			0		511 636	16891 9049	15622 16148
HT29 - 4							mutant		771	1454				409	13595	21159
HT29 - 5							mesternt		3498					1063	20245	27154
HT28 - 6 OVCAR-4 - 3	<del> </del>					-	mutant		3159	811		0		1090 229	5102	39150 12950
OVCAR-4 - 4							¥	0	3487		1105	_ 0	385	88	11844	11168
OVCAR-4 - 5							¥ 8	-	12920	1901	4206		907	375	8613	14155
OVCAR-4 - 6 SF339 - 3							wt	00	3819 6954	1285	706	00	1030	158	20409 8632	15714
SF539 - 4							w		11231	435		0	413	194	14688	10033
SF539 · 5							£ £		12548	396	469	_	642	352	4084	13577
SF\$39 - 6 OVCAR-5 - 3							mediani	- 0		296		- 0	1507	362 27	14823 i 8822	20785 14604
OVCAR-5 - 4							mutant	٥	3506		1061	0	948	488	8731	13868
OVCAR-5 - 6	<b></b>						Mutani		2838		69	0	766	105	319]	11271
ADR-RES - 6 MCF-7 - 6							mutant wt	-	3371 3709		1852 223	0	555	195	663)7 ( 20634	15034
Hela-8							HPV E6	٥	6165	0	2136	0	1130	874	28925	22168
H1299 - 6 SW480 - 3		<del></del>				$\vdash$	mutant mutant	00	1457 1242	70	5126	0	1106 393	304	60181 156161	16346
SW480 - 4							muturnt		4796		3609	- 0	461	543	47025	14272
SW480 - 5							mutent	•	7657	562	5967	0	1516	684	37625	16105
SW480 - 6 C33A - 3								00	4158 4870	0	1304	0	01	285 173	7118	17087
C33A - 4							ATTLACTOR I	0	2963		485 531	0	869	535	5045	7717
C33A · 5							(TALLET)		4227	126	2962	0	1128	454	11376	13418
C33A - 6 Ha68 - 6	<del></del>						enutural ref		1901 5858	9		0	467 561	656 535	9687 4849	17598
U2Q5 - 3					-		mutani					- 0		473	84995	18092
U2OS - 4							muteri	0	4249	2979	P596	٥	619	569	19448	17859
U2OS - 5					-	$\vdash$		0		4213	4861	0		478	39453	21270
U2OS - 6 WI 38 - 6							muteri wi	0			858	0	1963	389 540	2095	18157 12949
PHISS - 3							w		10577	10235	1233	0	2412	\$60	20617	13248
Hu68 - 4 SF-268-3							wi mulani		17277	1853				1992	29235 9499	20590
SF-268-4							mulani	. 0	4453 8837	760	11166	0	1910	925	16909	18347
SF-268-6							mulant	0	13125	0	2498		514	1137	278751	18866
SF-268-6	_						mutent	- 0	4068	0	0	Ō	368	406 852	2400 32105	18754
DePeng-13 Mikhai - 20								0		0	36386 4210	0	2461	740	11291	20203
Mitchell - Z1									14060		7219		24191	777	19057:	20805
Makhal - 22							7		13878		3119		2675	5971	15827	21250
OVCAR-5 - 5 Michael - 10					-	-	muteri					0	1167 2658	523 367	1837	15178 7630
Militari - 11 Militari - 12								0	6270	0	4706	C	937	129	688	4271
Michael - 12								0	10644		2689	0	Z250	926	43027	19005
Michael - 13 Michael - 14										0	1390	0		1229	575121 21693i	17026
Michael - 15									10792	. 0	3885	. 0	934	958	20174	15732
Michai - 16						$\Box$			7517	O	56	0	1777	710	18220	12001
Michail - 17 Michail - 18	<del></del>			<del>i</del>						0	296 224	0	1223	1438	1698 12985	16522 21852
Mahai - 19									9691		- 224		1173	649	22262	14100





180 Table 3 (contd)

			Turney - 3m - 17	umor cells	Normal IS	ndoe Ip	33 1:	SEQ 79 AA	SEQ DAZ- \$	SEQ 82 MU!	SEQ 84 RIAS	EQ 80 ANS	SEQ 89 AM	EQ 90 MS	SEQ 93 75	SEO 94 A
	umor-aym h	огта за-а ут	1 may - 10	166				279	236 69	18781 26330	1332	3003	782 <sup>2</sup> 4163	139	0	356
66-0				168				132	235	19539	3970	65	2558	414	0	
470				171		=		49	244	0	1622	1791		61	126	
83 1441 RNA 8/30	=		=	183	_			0 	204		321	111	01	0	0	26
817 untreated + ONess	+	<del></del>	<del></del>	194		ightharpoonup		114	- 6	541	2325	- 8	<u>S8</u>	101	190	
IS poly A*				196		$\rightarrow$		218	122	1363	3269	949	147	159	2	187
CHN				200		-		166	- 0	3977		2173	244	0	183	402 287
ACC-62 ACF-7/ADR-RES	<del></del>			293			=	100	0		330	215	140	252	124	49
/TOS (Mundy) poly e-				204	-+	<del></del>		112	269		637	315	a	0		157
VISH (Collegen) poly A+			+	206 208				1146	0	2134	2543	826	880 25	143	107	
S8 medulio mRNA CL 137 RNA 3/21/88				218							1884 3363	416	635	194	. 0	325
VL38 72N 0.5%FBS, 24N 10% FBS 1				219 270		-		- 5	154		177	0		5	71 94	
RL 1441 + TPA (24h) 8/30				· 221				18	55			144	0	133	- 6	22
(m-1				273		$\overline{}$	_	95	239		1182 622	0	- 11	24	0	127
Cart-4				725 241		+	-			1758	1886	983	185	216	40	
4OP-92				242				85	153		1028	2895 966	153	200	- 40	50
AOLT-4				243				0	226		2051		44	215		1 42
4.60				244 245			_	- 0			1403	0	700 57	225		
PM 8726				246			=		8			928	168	69		25
ASAWATCC				247		-			163		855	1682	589	17	. 0	
SR			<del>                                     </del>	248 249				0	145		1324	168	589	60		5 50
DVCAR-3 HCT-15				250				129			1486	201		0	167	7 10
DVCAR-4				251				171		307	480	0		. 0		1114
10-31			<del></del>	252 253				0	80	577	3409	0				2 43
DVCAR-S	<del> </del>			254				486	- 6			- 0	58			0 17
N12C DVCAR-8				255		<del></del>		181	2638		1953	3515	1363			4 52
OX MVI	<b>├</b> ───		H ———	256 257				140	73	32974	1309	565	126			6 44 7 12
GROVI	<u> </u>			258								1854 1949	561	_0	7.5	1 10
2K-0A-7				259	<b></b>	<del></del>		- 8		3676	172		26		41	1 16
SK-MEL-S	<b>├</b>		<del> </del>	260 261				159	0		1693	2596	925	496	174	13
SF-S39 SK-MEL-28				262		$\Box$		187			925	1578		74	40	0 20
K-562			<b></b>	263 264	<del> </del>	$\vdash$			63	6659	1900	175	91	109		0 12
UACC-257	<b></b>			265				0	21	1 1255	873 5288	3737 7090			<del> </del>	0 141
M14 MCF7				267		$\Box$		128				Q Q	147	290	121	614
MDA-MB-43S			<del>                                     </del>	269 270	<del> </del>	$\vdash$	_	38	24	6 0	1064	0	67	170	2	9 39
HT279	<del>                                     </del>			271							415	. 0			34	5 12
Y70 poly A+				273		$\vdash$	<u> </u>	11			6570	1854	211	1061		0: 216
KHOS goty A+	$\Box$			300	+			71		0 0	6206	9			15	7 34
HTB36 24h TPA RNA 6/23 HELA-EXP-031899				313				37				16718		690		0 4
HTB36 On RNA				322				292		0 59	4109	270	37	462	2 8	3 5
HT347	-			323	<del>                                     </del>	1		947	2 14	4 0	8157	6597			17	0 1
458 medulio RNA NCI-H226	<del></del> -		t	336				26		1 11463 0 10627		1515			9	ō 34
HOP-62			$\sqsubseteq$	337	<b>├</b>			833		7 131898		39722	955	1661	1 4	15 13
MDA-MB-231		<u> </u>	<del></del>	338	_			486	5 174	0 724467	8086	60552		1574		0 19
UZ\$1 PT culls poly A+	1		1	340				-		2 6025 5 25575	5 779 5 1044	16117	141	108	1	0 5
PC-3				341 343	<del> </del>	-		513		3 7505	1212	708	17	529	9	0 3
HCC-2998			<del> </del>	345	t			6	9	6 23824	1150	1491		2 24	<u></u>	0 5
SW-620 HT(92	<b></b>			346			<u> </u>	- 44	<del>} -  </del>	0 1595		634		<u> 48</u>	1	0
COLO 205			<b></b>	347	+				t l	0 612	5285	T	7	15		0 2
NT218 KM-12				349						1 8666		913	-			22 6
HT151				350				53	7 20	612		233	5	39		0 2
A498				351 352	+	<del>                                     </del>		23	5 13	)1	0 14919	180		2 21		0 3
HT393	┼──	<del></del>		353				35	0 163	0 9025			3 408		8 17	73 5
TK-10			$oldsymbol{ol}oldsymbol{ol}oldsymbol{ol}}}}}}}}}}}}}}}}}}$	355	₩-	<del></del>	<del>-</del>	142				51277	7 968		<u>ı                                     </u>	88 6
Mahme-3M		<del></del>	<del>                                      </del>	357	<del>                                     </del>			18	4	18 21180	0 1289		7 103			0 14
Ms 578T HTZ13			50			Ţ		14		0 64				9 59	4	0 19
HT288			52 54	<del> </del>	┼──	+	<del></del>	1 17			0 2329		0 5	<u>9j 30</u>	-	27 5
HT129	<del></del>	<del> </del>	54						0)	0 13			0 41		1	17 6
HT155 HT163			58		+	<del></del>	<del></del>	37	3	0 241	7 1494	186	al	0 71	9	0) 13
HT170	-	<del></del>	60	+	+			11	11}	8 9	5 2349	1			9	0 9
HT172 HT138	+		63			T		38	41 2	24 9 78 14				1	101	0) (
HT178			64	<u> </u>	<del></del>	+	<del>-</del>			0 37	4 2620		0	o ex	07	0 1
HT 154	+	<del>-</del>	65	+	1	<u> </u>		14	13 13	22 43	7 3689			<u>a </u>	0	82
HT180	<del>                                     </del>		67		$\vdash$	$\Box$	<b></b>		0 1	18 36 283	0 1861			id	13	78
HT 189			68_	<del></del>	+	+-	+	+ = =	27	0	0 2951	1			52	9
HT143	+	<del> </del>	<del>69</del> 70				1	36	52	71 136	6366			0 2		0
HT190 HT145			71		$\leftarrow$	+	+			68 208 0 21		3	0 10	15 41	54	0
HT227		<del></del>	72	<del> </del>	+	+	1	14	43	0 261	18 7386	6 185		77	21 1	0 1
HT302	+	<u> </u>	74					2	30	0 67				79 84	15 2	238 1
HT314 HT317		ļ	76		+	+	1		01	9 34	0; 2662	2	21	0, 0	68	0,
Markettestome 8425 11/8			77	+	+	$\perp$				0 50	05 4645	5			16	45
HT323 HT327	+	<del>                                     </del>	80			$\blacksquare$	=		0	<u> 27</u>	30 154; 0 4194			38	0	0
HT335	=		62	<b></b>	+	+	+	+	46		93] (	0	0	3.5	0 1	182
HT146	+	<del> </del>	85	+	$\pm -$	1			69 1	56 15	SO1 5529	9 :		17	51 1	111
HT348	+	<u> </u>	170			$\vdash$	$\vdash$	z	38		0 3176	61 61 161		0 3	82	0
HT398			185		+	+	+	+			01 (	0	0	0 1	80 1	159
HT140		<del>                                     </del>	187	+	+	$\pm -$			03	0	0 138	4 39	99		33 1	144
HT281	<del>                                     </del>		191		$\bot$	=	-	1	43 _2		0 271		0 2	0	10!	0
TCGP		-	207		+	+	+-	+'	94		80 139	5 34	06		40	0
HT 160	+		216	+	$\pm =$		1	1	0	80	0 222	2	01		49	115
HT307 HT369	+		224				$\vdash$	1 3	43	01	8 99 0 134		19	0	ol	0
H1370			226		+	+	+-	+	70 9	99	32 167	1	0		20	0
HT371	+	+	228 230	+	1		1		39 1	181 1	22 . 316	5			53	132
HT3/7	+	<del></del>	236				<b>T</b>	1	861		0 430				41:	0
nerucbiertome RNA			281			+-	+	+	0 1		0 679	1 13	82	65 1	23	0
НТЭЗИ			200	+	+	<del></del>			16	52	0 271	2	0 1			208
HT338	+	<del> </del>	315			$oldsymbol{\Box}$	$\top$		98	0 22	69 32 0 569	<u> </u>	54 1 0 9	01 1	66	0
MT392			317		+	+-	+		83 24 00	69 1	84 324	7	0	171	39 1	1501
HT392 HT394		<b></b>	319	+	$\pm$	$\pm -$		7 4	15	0 2	28 215	11	0	0	0	- 8
HT394 HT312											0 311			~1		
HT312 HT312 HT162	<del></del>		358		1		+						81 20	85	69	0
HT394 HT312 HT162 HT395 HT395					<del> </del>	=	+=	4	60	0	68 305	9 10 9 1785	81 25 78 36	85 1	13	0
HT394 HT312 HT162 HT395	163		358				E		37 1	0	0 441 68 305 19 601	9 104 9 1788 19 1575	81 26 78 36 62 14	85 16! 1	13	

WO 00/73469 PCT/US00/14842 ,

181 Table 3 (contd)

Hs 578T MCF-7/ADR-RES	Tumor-sym	Normal-sym	Tumor - to	Tumor calls	Normal	Endes	p33								SEQ 93 TS S	EQ 94 AIC
	155							235 454	156	133245 62599	4602 3763	2616801 173587	3072	326: 234	831	9393 4602
MCF7	151							0	96	22491	3645 5726	219251	402 734	463	56 78	\$546 8105
M14 UACC-257	149							34	190	44984	4498	46556	1177	177	77.	5052
UACC-62	145							- 0	103		8515 6515	4791B	1123 575	348	24	8145 1529
SK-MEL-28 UO-31	143							508	100	20649	9249	73274	520	189	275	4295 2500
SK-MEL-5 KM-12	142	-			-			104 416		3454	6756 3354	80653	109	127	162	3169
SK-MEL-Z	140							171	0	22819	3246 3913	134929	27	167	132	2792 7894
HCT-15	139							140			5765	137583	877	279	D.	3758
COLO 205	137	· · · · · · · · · · · · · · · · · · ·						0 158			5643 3350	114441	1470	9	74	5493 3197
LOX IMVI SW-620	136 135							168	- 0	11595	3617	104047	798	0	210	6275
TK-10	134							1060			4146 2016		1989	130 63	263	4536 7449
HCT 116	133							225	. 0	26315	3039	102477	3314	. 0	42	6256
HCC-2998	131					_		0			5568 4255		495 473	165	144	9603 2392
PC-3	129							160	104	8373	2715	90475	1017	248	65	7409 7546
RXF 393	128 127							134			3502 2431	59583 17433	377 259	298 54	0	2877
DU-145 C#4-1	126							0	141	60167	2648	64362	3136		471	5203
SR	125 124							0			2594 2600	91356	15	1182	o.	6992
A498 RPMI 8226	123							24	0	80	2614	12934	102	473 572	168	4276 11656
SN12C	122 121							513			7382 8301	450	369	314	173	21436
MOLT4	120										5372	83742		27 1262	171	3065
OVCAR-S K-562	119 116							425 258	9	10918	487	166477	2277	97	70	6579
OVCAR-4	117							654 D			2514 348	133148	8057 6977	231 144	0	3791 5240
OVCAR-J	116 115							464	37	13067	2669	95833	1585	33	0	3861
SF-539	114							217			388 1330	95279	2383 2689	110	0	5506 5448
HOP-62 SF-295	113							281	6	21130	3579	96198	3313	0	5	13804
AS49/ATCC SF-268	111							1009		23677	4014 291	126766	990	Z25 446	416	282
NGI-H522	109							364	213	33089	7465 5905	81138	3557	225 183	113 253	4120 731
U251 NCI-H460	108							29Z 170		27031	269	46575	3614	27	5	420
SN8-75	106					=		0		5661	186	66012	1698	143	8	6291 5616
NCI-H322M SNB-19	105							212 139	56	6406	298	17270	1903	0	87	6176
NCI-H226	103						$\vdash$	21 <u>1</u>	115		5630 238		4063 5044	212	171	10900
NCI-HZ3	101							319	432	61716	299	2376	1016	187	64 215i	9311
IGROV1	100	-						62	137	6156	458	5729	613	373	0.	675
OVCAR-6	98							106	73	5123	539	5 2969	2072	116 305	9	9101
HOP-92 h feroblesia 3/31/92 #12	48		-				-	315	260		676	190645	4899	414	0!	486
n adult SMC 10/21/92 #17	47							0		1880				456 117	264	438. 576
h kerannocytes 2/25/92 #10 TCGP	46 26							0	16	11006	623	81465	341	226	10	1413
Á549 - 1							wi.	0					3072		48 276	99
A549 - 3 A549 - 4	<u> </u>	<u> </u>					w1	. 0	6,	116	4624	7	1843	0	342	75
A549 - 5							wi				7256 1986	7 0	2142	•	- 8	137
A549 + 7 EKVX + 1							MURRIN		280			1 0	4755	0		169
EKVX - 4 EKVX - 3	ļ						mutent	0		49	7779	8 0	6784	Ó	0	82
EKVX - 5							muteril materil	8	10	1208	3763	1 0	898			220 456
EKVX - 7 MCF-7 - 1	<del> </del>						wt		550	0	4158	1 0	322	0	. 0	118
MCF-7 - 3							wt				3764 3208	2 0	648		124 91	
											2597	5] 0	680		1001	
MCF-7 - 4 MCF-7 - 5							w	-					- 900			- 65
MCF-7 - 5 MCF-7 - 7							wi muteni		74	1610	6943	5 0	2747	. 0	912	177
MCF-7 - 5							wi muteni muteni	0	25- 74- 9 91	1 20 1 1610 1 2497	4385	5 C	2747 2747	0	0 912 175	177 112
MCF-7 - 5 MCF-7 - 7 ADR-RES - 1 ADR-RES - 3 ADR-RES - 4							wt muter/	0 0	25- 74- 9 91 9 44:	20 1610 1 2497 9 218	4385 4063 3054	5 0 2 0 7 0 7 0	0 2747 0 860 0 1142 0 1779	0 0 0	0 912 175 0	69 177 112 142 24
MCF-7-5 MCF-7-7 ADR-RES-1 ADR-RES-3 ADR-RES-4 ADR-RES-5 ADR-RES-5 ADR-RES-7							wi mutani mutani mutani mutani mutani	0 0 0 0 0	25- 74- 91 91 9 44:	4 20 4 1610 1 2497 9 218 0 4	4385 4363 4063 3054 2794	5 0 2 0 7 0 7 0 5 0	0 0 2747 0 860 1142 1779 1 1085	0 0 0	0 912 175 0 24	69 177 112 142 24 92
MCF-7-5 MCF-7-7 ADR-RES-1 ADR-RES-3 ADR-RES-4 ADR-RES-5 ADR-RES-7 WI 38-1							wi muteni muteni muteni muteni	000000000000000000000000000000000000000	25- 74- 91 44- 1 47- 1 95- 1 36-	20 1 1610 1 2497 9 218 0 4 0 4304 1 3364 2 1018	6943 4385 4063 3054 2794 6792 4567	5 0 2 0 7 0 7 0 5 0 1 0	0 0 2747 0 860 0 1142 0 1779 1 1085 0 19059	0 0	0 912 175 0 24 0 110	69 177 112 142 24 92 204 130
MCF-7: 5 MCF-7: 7 ADR-RES: 1 ADR-RES: 3 ADR-RES: 3 ADR-RES: 5 ADR-RES: 5 ADR-RES: 5 MI38: 1 WI38: 3 WI38: 3							wi mutani mutani mutani mutani wi wi	000000000000000000000000000000000000000	25- 74- 9 91 0 44- 1 95- 1 95- 1 36	4 20 4 1610 1 2497 9 218 0 4 3 4304 1 394 2 1018 0 1422	4385 4063 3054 2794 8792 4567	5 0 2 0 7 0 7 0 5 0 1 0 1 0	0 0 2747 0 860 0 1142 0 1779 1 1085	0 0	0 912 175 0 24 0 110 0	69 177 112 142 24 92 204 130 123
MCF-7 - 5 MCF-7 - 7 ADR-RES - 1 ADR-RES - 3 ADR-RES - 4 ADR-RES - 4 ADR-RES - 7 W130 - 1 W130 - 3							wi mutani mutani mutani mutani mutani wi wi wi	000000000000000000000000000000000000000	25 74 9 91 47 1 95 1 36	4 20 4 1610 1 2497 9 218 0 4 0 4304 1 3394 2 1018 0 1422 5 1554 7 365	6943 4385 4063 3054 6792 4567 4406 4854 3297	5 0 2 0 7 0 7 0 5 0 1 1 0 1 1 0 3 0 3 0	0 0 0 0 2747 0 0 0 0 1142 0 1779 1 1085 1 19059 1 19258 1 9336 1 7404 1 10729	000000000000000000000000000000000000000	0 912 175 0 24 110 0 0 0 0	59 177 112 142 24 92 204 130 123 105
MCF7-5 MCF7-7 ADR-RES-1 ADR-RES-2 ADR-RES-2 ADR-RES-3 ADR-RES-5 ADR-RES-5 MCP-RES-5 MCP-RES-5 MCP-RES-7 W/ 38-3 W/ 38-3 W/ 38-3 W/ 38-5 W/ 38-7							wi mutani mutani mutani mutani wi wi wi wi wi	000000000000000000000000000000000000000	26-74-91 91 94-91 95-95-95-95-95-95-95-95-95-95-95-95-95-9	4 20 4 1610 1 2497 9 218 0 4 3 4304 2 1018 0 1422 7 365 7 365	6943 4385 4063 3054 2794 6792 4567 4408 4854 3297	5 0 2 0 7 0 7 0 5 0 1 0 1 0 3 0 3 0 6 0	0 0 0 2747 0 000 0 1142 1779 1 1085 1 19059 1 10258 1 9338 1 7404	000000000000000000000000000000000000000	0 912 175 0 24 110 0 0 110 0 0	69 177 112 24 26 92 204 133 12: 10: 10: 11:
MCF7-5 MCF7-7 ADR-RES-1 ADR-RES-3 ADR-RES-3 ADR-RES-3 ADR-RES-5 ADR-RES-5 ADR-RES-5 MI 38-1 WI 38-1 WI 38-1 WI 38-1 WI 38-3							wi mutant mutant mutant mutant wi wi wi wi wi wi HPV E6 HPV E6	000000000000000000000000000000000000000	25- 74 91 94 94 147 95 36 15 17 26 17 26 19 26 19 19 19 19 19 19 19 19 19 19 19 19 19	1 20 1 1610 1 2497 9 218 9 4304 9 3 4304 9 3394 9 101 1 1422 8 1554 7 363 7 0 9 1254	4343 4385 4063 3054 2794 6792 4567 4408 4854 3297 4979	\$ 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 2747 0 860 0 11142 0 1085 0 1085 0 10258 0 10258 0 10729 0 10729 0 957 7 756	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0   912   175   0   0   0   0   0   0   0   0   0	69 177 112 24 92 20 133 105 105 111 84
MCF7: 5 MCF7: 7 ADR-RES - 1 ADR-RES - 2 ADR-RES - 2 ADR-RES - 2 ADR-RES - 7 W130 - 1 W130 - 1 W130 - 1 W130 - 5 W130 - 7 HMA - 7 HMA - 7 HMA - 3 HMA - 4 HMA - 5							with muteri muteri muteri muteri muteri muteri muteri wi wi wi wi wi wi hipv E6 HPV E6 HPV E6 HPV E6 HPV E6	000000000000000000000000000000000000000	25- 74 91 94 1- 95- 36 1- 1- 1- 1- 1- 1- 1- 1- 1- 1- 1- 1- 1-	1 20 1 1610 1 2497 9 218 9 218 9 3 4304 9 430 1 3394 2 1018 1 1554 7 365 7 0 0 331 1 254 0 330 1 420 1 1422 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	4385 4063 3054 2794 4567 4408 4854 4954 4979 3807 4979 4144 4737 4983	S	0 0 0 0 2747 0 860 0 1142 0 1772 0 1085 0 19059 1 10256 1 10256 1 10256 1 10256 1 10729 1 1	000000000000000000000000000000000000000	0 912 175 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	69 177 112 142 24 92 204 130 105 105 111 84 52
MCF7-15 MCF7-17 ADR-RES-1 ADR-RES-2 ADR-RES-2 ADR-RES-3 ADR-RES-3 ADR-RES-3 W130-1 W130-1 W130-1 W130-1 W130-1 W130-5 HM4-1 HM4-1 HM4-1 HM4-1 HM4-1 HM4-1							with mutant mutant with with with with with with with wit	000000000000000000000000000000000000000	25- 74- 91 91 447 95- 36 11 26 12 26 14 16 16 16 16 16 16 16 16 16 16 16 16 16	1 20 1 1610 1 2497 9 218 9 218 9 218 9 218 9 218 9 430 1 3394 1 1018 1 1	4385 4063 3054 6792 4567 4408 4854 3297 3907 4979 4144 7377 4989 2277	S 0 2 2 0 7 7 0 7 7 0 0 1 1 1 0 0 1 1 1 0 0 1 1 1 1	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	01 912 175 0 0 24 10 0 0 10 0 0 169 140 0 0 0 151	69 177 112 142 24 92 204 130 105 105 111 84 52 53
MCF-7 - S MCF-7 - T ADR-RES - 1 ADR-RES - 3 ADR-RES - 3 ADR-RES - 5 ADR-RES - 5 ADR-RES - 5 ADR-RES - 5 MU 36 - 3 WU 36 -							with muters muters muters muters with muters with with with the muters with th	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	25-74-75-75-75-75-75-75-75-75-75-75-75-75-75-	1 20 1 1610 1 2497 9 218 0 4304 0 4304 0 4304 0 1422 10 18 0 1422 7 365 7 0 3030 8 84 6 84 7 330 6 84 7 330 6 84 7 330 6 84 7 330 6 84 7 330 6 84 7 330 6 84 7 330 7 330 7 34 7 35 7 4 35 8 8 5 8 8 5 8 8 6 8 8 6 8 8 6 8	4343 4365 4063 3054 6792 4567 4408 4854 3297 4979 4144 7377 4865 2277 4863 3350	S 0 0 0 7 0 0 7 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	01 912 175 0 175 0 1 100 0 0 0 0 0 1 100 1 100 1 100 0 0 1 100 0 0 1 100 0 0 0	650 650 1171 1172 142 24 20- 132 102 102 103 104 104 105 1111 1
MCF7-5 MCF7-7 ADR-RES-1 ADR-RES-3 ADR-RES-3 ADR-RES-3 ADR-RES-5 ADR-RES-5 ADR-RES-5 ADR-RES-5 ADR-RES-7 W138-3 W138-1 W138-7 NU38-7 NU38-7 NU48-3 NU48-3 NU48-7 NU4							with mutant mutant mutant with with the policy of the poli	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	25-5 74- 91 91 441 1 445- 1 35- 1 36- 1 14- 1 26- 1 14- 1 15- 1 26- 1 15- 1 16- 1 16- 1 174 1 15- 1 15	1 20 1 12497 1 2497 2 2 8 2 3 4304 3 4304 2 1018 5 1554 7 365 7 0 3 1254 0 1425 0 1425 0 1425 1 1555 1 1554 1 1554 1 1070 1	4365 4063 3054 6792 6792 4567 4408 4854 3297 3307 4979 4144 7377 4089 2277 2613 3555 1545	S 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 2747 0 860 0 1142 0 1959 0 1085 0 19059 0 19059 0 19059 0 19059 0 19059 0 19059 0 19059 0 19059 0 19059 0 19050 0 190	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0   912   175   17	650 1777 1172 144 24 200 200 133 122 100 100 111 84 55 55 111 111 44 44 40 40 45 45 45 45 45 45 45 45 45 45 45 45 45
MCF7-5 MCF7-7 ADR-RES-1 ADR-RES-2 ADR-RES-3 ADR-RES-3 ADR-RES-3 MP-RES-3 MP-RES-4 MP-RES-4 MP-RES-4 MP-RES-4 MP-RES-1 MP							with mutant mutant mutant mutant with with with the mutant with the mutant with the mutant mu	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	256   144   147	1 200 1 160 1 161 2 170 1 2497 9 216 9 216 9 216 9 216 1 3984 2 1018 1 3984 2 1018 1 1554 6 6 60 0 142 1 107 4 1872 0 86 3 4672 0 86 3 4672	\$943 43655 4063 3054 4567 4567 4408 4854 4397 3907 4979 2277 2513 2513 2513 2513 2513 2513 2513 2513	S	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	01 912 175 0 24 110 0 0 1 0 1 0 1 0 1 0 1 0 1 0 1 0 1 0	650 1777 1112 242 292 200 122 100 101 111 111 94 44 44 46 155 55 55 55 55
MCF7-5 MCF7-7 ADR-RES-1 ADR-RES-2 ADR-RES-3 ADR-RES-3 ADR-RES-5 ADR-RES-5 ADR-RES-5 MF							well musters! musters! musters! musters! musters! well well well well well well well wel	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	25-5   25-5	200   200	\$943 43655 40630 3054 5792 4408 4408 4254 3207 33007 3307 4144 4929 2277 4949 2277 2413 3550 3550 3557 3557 3557 3557 3557 355	S Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q	0 0 0 0 2747 0 2650 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0   912   912   175   17	650 1777 112 144 242 29 29 132 122 100 100 100 100 100 100 100 100 10
MCF7-15 MCF7-17 ADR-RES-1 ADR-RES-1 ADR-RES-2 ADR-RES-2 ADR-RES-3 ADR-RES-3 M138-1 W138-1 W138-1 W138-1 W138-1 H138-7 H44.a-1 H45.a-1							wei mutent mutent mutent mutent mutent wil wil wil wil wil wil wil wil wil wil	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	25-5 25 25 25 25 25 25 25 25 25 25 25 25 25	200   200	\$943 4355 4053 4053 2754 4577 4400 4575 4400 4575 4107 4107 4107 4107 4107 4107 4107 4107	\$ 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 27.7 0 860 0 1 17.7 0 1 10.5 0 1 17.7 0 1 10.5 0 1 17.7 0 1 10.5 0 1 17.7 0 1 1 10.5 0 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0   0   0   0   0   0   0   0   0   0	65 1777 112 144 242 290 135 127 100 100 100 101 111 44 400 400 55 55 55 55 55 55 55 55 55 55 55 55 5
MCF7-15 MCF7-17 ADR-RES-1 ADR-RES-1 ADR-RES-2 ADR-RES-3 ADR-RES-3 ADR-RES-3 MDR-RES-1 WI 30-1 WI 30-1 WI 30-1 WI 30-1 WI 30-1 WI 30-1 HM-1-3 H							with mutant mutant with with with the public properties of the public p		25-5 25-5 25-5 25-5 25-5 25-5 25-5 25-5	200   200	\$943 4365 4065 4065 5792 4507 4406 4507 4977 4985 2277 2813 297 2813 297 297 297 297 297 297 297 297 297 297	\$ 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 200 0 200 0 200 0 0 0 0 0 0 0 0		0 0 0 170 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	65 1777 1112 242 242 293 134 122 100 100 100 100 100 100 100 100 100
MCF7-15 MCF7-17 ADR-RES-1 ADR-RES-13 ADR-RES-2 ADR-RES-3 ADR-RES-3 MDR-RES-3 MDR-RES-15 WI 38-3 WI 38-3 WI 38-3 WI 38-1 WI 38-3 WI 38-4 WI 38-3 WI 38-6 WI 38-7 Held-1 Held-3 Hel							wit mutani mutani mutani mutani mutani wi wi wi wi wi wi wi wi wi wi wi wi wi		25-5 25-5 25-5 25-5 25-5 25-5 25-5 25-5	200   200	69-13 436-55 4063 305-54 4063 4567 44000 329-75 4000 329-75 4000 4000 4000 4000 4000 4000 4000 40	\$   0   2   2   0   7   7   0   7   7   0   7   1   1   1   1   1   1   1   1   1	10 0 0 27.7 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0		0 0 0 0 1750 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	65 1777 1114 142 242 293 290 113 122 110 100 111 111 111 111 111 111 111
MCF7-7 S MCF7-7 ADR-RES -1 ADR-RES -1 ADR-RES -3 ADR-RES -3 ADR-RES -5 ADR-RES -5 ADR-RES -5 W130 -1 W130 -1 W130 -1 W130 -1 W130 -1 W130 -1 H130 -1 H							ord mutant mutant mutant mutant mutant will will will help E6 help E6 mutant mutant mutant mutant mutant will will mutant will mutant will mutant will mutant will mutant will mutant will mutant will mutant will mutant will mutant mutant will will mutant will will mutant will will mutant will will will will will will will wil		25-5-5-5-5-5-5-5-5-5-5-5-5-5-5-5-5-5-5-	200   2497   1	69-13 430-55 400-33 30-54-56 400-33 456-76 400-35 4	\$ 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	10 0 0 2747 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1		0 0 1912 110 110 110 110 110 110 110 110 110 1	65 1777 1114 144 29 29 136 137 100 100 100 111 100 100 100 100 100 10
MCF7-15 MCF7-17 ADR-RES-1 ADR-RES-1 ADR-RES-2 ADR-RES-2 ADR-RES-2 MD-RES-2 MD-RES-2 W138-1 W138-1 W138-1 W138-1 W138-1 H138-1 H1							wit muters muters with the property and		25-5 25-5 25-5 25-5 25-5 25-5 25-5 25-5	200   200	6943 4365 4063 3054 4063 4567 4567 4406 4854 4277 3807 4947 4947 4947 4947 4947 4947 4947 49	\$ 2 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	10 0 0 2747 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 9 175 1	55 1777 1114 142 22 29 132 100 1111 81 99 40. 155 55 55 1111 1112 1112 1112 1112 111
MCF7-7 S MCF7-7 ADR-RES -1 ADR-RES -1 ADR-RES -3 ADR-RES -3 ADR-RES -3 ADR-RES -4 ADR-RES -5 ADR-RES -5 MCR-RES -5 ADR-RES -5 MCR-RES -6 MCR-RES -6 MCR-RES -6 MCR-RES -6 MCR-RES -6 MCT-RES -6 MCT-RES -7 AS40 -2 EVXX-2 MCT-RES -7 AS40 -2 EVXX-2 MCT-RES -7 AS40 -2 EVXX-2 MCT-RES -7 AS50 -2 SF-RES -7							wit mutant mutant wit wit wit wit wit wit wit wit wit wi		25-52-52-52-52-52-52-52-52-52-52-52-52-5	200   2497   1	69-13 436-55 4063 305-54 4063 4567 4406 485-4 407 3007 4973 4943 2277 2713 2713 2713 2713 2713 2713 271	\$ 2 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0   0   2747   1   1   1   1   1   1   1   1   1	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 9 175 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	65 177 1144 22 29 20 150 150 160 160 160 170 160 170 170 170 170 170 170 170 170 170 17
MCF7-7 S MCF7-7 ADR-RES -1 ADR-RES -1 ADR-RES -3 ADR-RES -3 ADR-RES -4 ADR-RES -4 ADR-RES -5 ADR-RES -5 MCR-RES -5 ADR-RES -5 MCR-RES -7 WI 38 - 3 WI 38 - 5 WI 38 - 7 Held - 1 Held - 3 Held - 1 Held - 7 Held - 7 Held - 7 HERO - 7 AS49 - 7 HERO - 7 AS49 - 2 EVXX-2 HCT-116 - 1 HCT-116 - 7 HCT-11							ori mudent troutent mudent mudent mudent mudent with the properties of the propertie		26-12 26-12	200   200	8943 4365 4063 4063 4063 4567 4567 4567 4567 4567 4567 4567 4567	\$ 2 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 277.7  10 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0		0   912   175   17	65 177 1144 22 29 20 150 150 160 160 160 170 160 170 170 170 170 170 170 170 170 170 17
MCF.7: S MCF.7: S MCF.7: T ADR.RES - 1 ADR.RES - 1 ADR.RES - 3 ADR.RES - 3 ADR.RES - 3 ADR.RES - 3 MCF. S M							ori mudent troutent mudent mudent mudent mudent with the second mudent with the second mudent mudent with the second mudent with the second mudent mudent mudent mudent with the second mudent mudent mudent with the second mudent mudent mudent mudent mudent with the second mudent mudent mudent with the second mudent mudent with the second mudent mudent mudent with the second mudent mudent with the second mudent mudent with the second mudent		26-64   26-6	200   249	89-13 430-55 405-55 405-55 405-56 405	\$ 2 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	10 0 0 2747 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1		0 0 175 175 175 175 175 175 175 175 175 175	65 1777 112 1442 2202 2002 122 100 100 101 111 111 111
MCF7-1'S MCF7-1'S MCF7-1'T ADR-RES-1 ADR-RES-1 ADR-RES-3 ADR-RES-3 ADR-RES-1 MDF-RES-1 ADR-RES-2							ort muteral structural		26-64   26-6	200   2407   2	69-13 439-5 439-5 439-5 439-5 439-5 439-5 439-5 439-7	\$ 2 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0		0 0 175 1 17	65 1777 1112 1442 229 290 1122 1101 1111 1111 1111 1111
MCF.7: S MCF.7: S MCF.7: S ADR.RES. 1 ADR.RES. 3 ADR.RES. 3 ADR.RES. 5 ADR.RES. 5 MI. 30 - 1 WI. 30							ort muters! or muters!		26-64   26-6	200   200	69-12 439-5 4053 4053 4053 4179-2 417	\$ 2 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0		0   912   175   17	66 17 17 17 17 17 17 17 17 17 17 17 17 17
MCF.7: 5 MCF.7: 7 ADR.RES - 1 ADR.RES - 1 ADR.RES - 2 ADR.RES - 2 ADR.RES - 3 ADR.RES - 3 ADR.RES - 3 MD.RES - 3 MD.RES - 3 MD.RES - 3 MD.RES - 7 WI 38 - 3 WI 38 - 3 WI 38 - 3 WI 38 - 5 WI 38 - 1 HI 38 - 7							ori mutanti mu		28-52   28-5	1	69-12 436-5 406-5 579-2 679-2 4400 4400 450-7 320-7 30	\$ 2 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	10 0 0 2747 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0		0 0 1 175 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	66 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6
MCF-7'-5 MCF-7'-7 ADR-RES-1 ADR-RES-1 ADR-RES-3 ADR-RES-3 ADR-RES-3 ADR-RES-1 MI 30-1 WI 30-1 WI 30-1 WI 30-1 WI 30-1 WI 30-1 WI 30-1 HI 30-1							ort motions of the control of the co		28-9   28-9	1	69-12 426-5 406-5 579-2 4406-6 4406-6 4406-6 4406-6 40	\$ 2	10		0 0 1912 175 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	66 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6
MCF-7: S MCF-7: S MCF-7: S MCF-7: T ADR-RES: 1 ADR-RES: 1 ADR-RES: 3 ADR-RES: 5 ADR-RES: 5 MCF-7: T W130 -1 W130 -1 W130 -1 W130 -1 W130 -1 W130 -1 W130 -1 H130							ort muteral muteral with the product of the product		28-6   28-6	1   200	69-12 69-12	\$ 2 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	10		0   912   175   17	66 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6
MCF-7: S MCF-7: S MCF-7: T ADR-RES: 1 ADR-RES: 3 ADR-RES: 3 ADR-RES: 3 ADR-RES: 3 MCF-7: S MC							ort modern's modern's modern's with the property of the proper		28-0   28-0   1   1   1   1   1   1   1   1   1	1	69-12 405-3 406-3 406-3 67-92 406-3 40	\$ 2 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	10		0   912   175   17	66: 6: 6: 6: 6: 6: 6: 6: 6: 6: 6: 6: 6:
MCF7-1'S MCF7-1'S MCF7-1'T ADR-RES-1 ADR-RES-1 ADR-RES-3 ADR-RES-3 ADR-RES-3 ADR-RES-1 M138-1 W138-5 W138-1 W138-5 W138-1 W138-5 W138-7 Held-1'S He							ort muteral muteral with the property of the p		26-64   26-6	1   200   24071   1   1   1   1   1   1   1   1   1	69-13 405-3 40	\$ 2	0		0   912   175   17	66 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6
MCF-7: S MCF-7: T ADR-RES -1 ADR-RES -1 ADR-RES -3 ADR-RES -3 ADR-RES -5 ADR-RES -5 MD -1 W130 -1 W130 -1 W130 -1 W130 -1 W130 -1 W130 -1 H130 -1 H130 -1 H120 -1							ort modern's modern's modern's with modern's with the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's modern's modern's modern's modern's modern's will be a seen of the modern's modern's modern's modern's modern's modern's modern's modern's modern's will be a seen of the modern's modern'		28-0   28-0   14-0   15-0	1   200	69-12 430-5 4053 4053 4053 41792 417	\$ 2 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0		0   912   175   17	66 67 77 77 77 77 77 77 77 77 77 77 77 7
MCF-7: S MCF-7: S MCF-7: T ADR-RES: 1 ADR-RES: 1 ADR-RES: 3 ADR-RES: 3 ADR-RES: 3 ADR-RES: 3 MOI-10-10-10-10-10-10-10-10-10-10-10-10-10-							ort modern's modern's modern's with modern's with the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's modern's modern's modern's modern's modern's will be a seen of the modern's modern's modern's modern's modern's modern's modern's modern's modern's will be a seen of the modern's modern'		28-52   28-5	1	69-12 69-12	\$ 2 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0		0   912   175   17	66 6 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7
MCF7-1 S MCF7-1 S MCF7-7 ADR-RES - 1 ADR-RES - 1 ADR-RES - 2 ADR-RES - 3 ADR-RES - 3 ADR-RES - 3 ADR-RES - 3 MD - 1 MD -							ort modern's modern's modern's with modern's with the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's modern's modern's modern's modern's modern's will be a seen of the modern's modern's modern's modern's modern's modern's modern's modern's modern's will be a seen of the modern's modern'		276-20   2	1	69-13 405-3 40	\$ 2	0		0   912   175   17	66 67 77 77 77 77 77 77 77 77 77 77 77 7
MCF-7: S MCF-7: S MCF-7: T ADR-RES: 1 ADR-RES: 3 ADR-RES: 3 ADR-RES: 3 ADR-RES: 3 ADR-RES: 5 ADR-RES: 5 MD 30: 1 W130: 1 W130: 1 W130: 1 W130: 1 W130: 1 W130: 1 H130: 1 H130: 1 H130: 1 H120:							ort modern's modern's modern's with modern's with the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's modern's modern's modern's modern's modern's will be a seen of the modern's modern's modern's modern's modern's modern's modern's modern's modern's will be a seen of the modern's modern'		28-0   28-0   1   1   1   1   1   1   1   1   1	1	69-13 405-3 40	\$ 2	0		0   912   175   17	66 67 77 77 77 77 77 77 77 77 77 77 77 7
MCF-7: 5 MCF-7: 5 MCF-7: 5 MCF-7: 7 ADR-RES: 1 ADR-RES: 3 ADR-RES: 3 ADR-RES: 3 ADR-RES: 3 MCF-7: 8 MCF-7: 8 MCF-7: 9 MC							ort modern's modern's modern's with modern's with the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's will be a seen of the modern's modern's modern's modern's modern's modern's will be a seen of the modern's modern's modern's modern's modern's modern's modern's modern's modern's will be a seen of the modern's modern'		26-64   26-6	1   200	69-12 69-12	\$ 2 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0		0   912   175   17	6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6

182 Table 3 (contd)

							5-4 7	-45 Is	FO 78 AA	SEG GOZA M	SEQ 82 MUS	EO M ROSE	O BE AN SI	O BY AN SEG	90 M 9 SE	Q 93 TS S	EQ M AC
		Tumor-sym	Normal-sym	Tumor - 10	Tumor cells	Norm ut	2000			1167	22871	94067		72321			1528 623
	Pro-7									2758						103	750
	ePang-9									- 22		73585	0	8754			1249 1770
	Perg-11	<u> </u>	<b></b>						- 0	0				10777		0	515
	aPang-10									257			- 6	Z318			300
	aPeng-1								0	406	205			1211			393 584
	aPeng-Z							$\rightarrow$		213	561			559	ō	354	801
	P#94					_				2655	0	45709		01			627 492
String	-O		<del>   </del>							1846							545
	549 - 8					-	<u> </u>			164			6	7705			2322 1568
Color   Colo	KVX · 6	<u> </u>		$\vdash$						173	636	22256					1781
Color   Colo	CT-118 - 7									205	1301	47637			01		652
Color   Colo	fT29 · 1				<b></b> -		<del></del>	mutent		0	80						441
Section	(129 · /		$\vdash =$					mutant		45				1532	0		933
1985	F539 - 7				<del> </del> -	<del></del>				1007	1761	38166		4116			1851
1.   1.   1.   1.   1.   1.   1.   1.	F 539 - 8	<b></b>						mutent			2013	52411		41301			1371
Control	F-268-8					<del> </del>	<del> </del>	mutent _				24881	0	534	0		768
Control   Cont	DVCAR-4 - 7	<del></del>	<del></del>	<del> </del>				-4			2400	56208		2132			3745
Control	DVCAR-5 - 7						$\sqsubseteq$				476	13621;	01		0 i_	- · · · · · · · · · · ·	571
	DVCAR-5 - B		<del> </del>	<del></del>	<del> </del>	<del> </del>	$\vdash$	lwa .		204	0	40597					342 1207
Table     Tabl	ADR.RES - 8	<del></del>						mutant				21952		564	0	269	651
Table	HeLa · 8				<del></del>	<del> </del>	<del>                                     </del>			235	483	28435	- Ò	1176		89	1435
	SW480 - 7		<del>                                     </del>					mutant			- 0	27332			0	53	724 650
Color   Colo	H1299 - 8		$\vdash$		1	+	+	Markey.		1006	204	19611		91	_01		650 1883
	C33A - 7	+	+	<del></del>	<del> </del>		上二	areatent.		0 7777	323	70434		33861	- <del></del>		979
100   1	U2QS • 7							anutani			826	33247	01	112		36,	858
Main   Main	U2OS - B			<del> </del>	+	+	<del></del>	w		0 88	522	76356			- 0		855 1105
The color of the	Har68 - 6	<u> </u>						wt				82606		142	0	01	960
Characterists	W1 36 - 5		1		+	+	+-	<del> "</del> -			16715	14760	157513	8551			2436 2241
Company   Comp	458 medulio RNA	+	+	上二							154	1378			254	0	12872
Tright	Bard		Ţ	ļ		+-	<del>                                     </del>	<del>'</del>		0 3		4338	137	22	590		7852 3943
1732   1732	H17368	+	+	t				1		0 30	0	4042		1123			10627
1725   172   173   175					=	=		+		9 185	974	5319	0	287	356		6483
Section   177	HT308	$\overline{}$	<u> </u>	<del> </del>	+	+	173	$\pm$	10	5		1494		- 0			4067
Description		1					175	$\overline{}$				1799		54	0		3483
The company   Company	Ber-9			<del> </del>	<del></del>	+	11/			0	0	2152	2734	9	61		5086 2460
Tributa	h turninocytes 2/25/92 #10	+	<b>—</b>	1			237	-		7 5	621			165		6	1021
	HTB10					+	+	+		0	391	2370		510			1882 474
Case   Case			+	t				T						495			12886
Second part   Second part	MNNG-OS poly A.				+	+	+	+-		12	3011	1291	6062	49			6785 4771
Mathematics   Mathematics	SA-OS (Mundy) poly A+	+	+	+	1				6	30	7825						0
	HCT-116 - 3						+-		+		234	30197	. 0	5246			307 1024
Color   Colo			+		+			w		al	7 37			1996		- 66	1306
Add						1	+-		+	8 - 19	61 0	21797	0	0		. 0	907
Total				+	+	+	1			0 30				193		159	969
						$\blacksquare$	=		+	0 13				464	0		2528
Fig. 2	HT29 - 4					+	+		1	0 3	1 1353	76872					1325
OyCARA 1		+	- I.	1					-	0 47						٥	879
DOCATAL 1	OVCAR-4 - 3		7	Ţ		-+	+-		<del>                                     </del>	0 43	8 397	30765				- 65	1006
Company   Comp				+						0 10					- 0	515	1083
SFAIL						+	+		+	B 11		32560			- 0		125
SFEST		+	+		-			w				27211				236	
SF430 - 6								<u> </u>				59630	- 0	0		262	82
DYCARS-3	SF\$39 - 6		<del></del>	+	+	+-			1	0 16	667	27675					
DOCAR-9-6		上二				=	=	mutant	+			9373		4831			47
MCG-7- 6	OVCAR-5 - 6			<del></del>	+	+-		mutan	土二	0	8	7 24265	<u> </u>				
Hall   High   S		<del></del>						- I						1196			96
Hill 29 - 5	Hale 6					+-	+			D	0 0	0 26441		4028			
SWIND 1   SWIN	H1290 - 6							mut and			57 44	4 24371	<del>                                     </del>	2235	0		101
SW180 - 5	SW480 - 4	$\bot$									45 66	4 52347		5885	0	26	157
	SW480 - 5	<del></del>	+					muteri			120	7 31434	<del>  }</del>	1873		3	2 16
CSBA -	C33A - 3			=				mutani			29 15	5 28446		368		1	
CASA-	C33A - 4		+	+	+			mutan		0 16	55 71	1 296532					
Helds   B				=				mutan	4			0 23074	·I	0101	0	12	3: 41
UCSS-3	Pta66 - 6		-	$+$ $\equiv$	+	-+	+	maken		0	58 264	7 52225	<u> </u>				
USSS 5							$\Rightarrow =$	muten				4 50322	<del>                                     </del>			12	0 125
UCS3-6	U205 - 5		7					mulari	<del>     </del>	öl	44 35	9 25411		93			0 174
He66 : 1				+				wt	4			O 1676					0 93
He66 - 1	Ha68 - 3					7=	-	- 5				6 5886	2	0 10191		48	
SF-788-3	He68 - 4	-		+		_		mager	4	0 1	11 14	8 4720	ST				
\$57,786-5	SF-268-4					=		mustan						0 8455			0 11
Street   S	SF-268-S	$\dashv$				+-	-+-			0	0 90	4 2768					0 8
Medical - 27		<del></del>				$\exists =$		=		0		136780				21	3 70
Method: 21   0 0 0 0 118555 0 0 533 0 0 0 0 0 0 0 0 0 0 0 0 0 0	Michael - 20							-+	+	8	0	0 9676	51	0 6661		11	41 11
MASH				+		$\pm$	$\perp$	=		0	0	0 11856	3	0 6553			0 5
Manual : 10		士二					$\perp$	muten	4	0		0 2740	9	0 686		0	0 4
Mahoud   17	Mitthell - 10			+	+	_	+		$\pm$	_0	12	1 1604	4	0 232		91 3	0 11
Machael 1   3   0   0   0   0   0   0   0   0   0							$\bot$	丰	4	0						0]	4 9
Method: 14   0   9   0   98133   0   6251	SANCHINE - 13	=		$\mp$				-+	+	0	93	16 9662	6	0 6687			
Martinal   15   0   0   0   0   0   0   0   0   0		+	-+		+-					01	- O						73 10
Mehnal : 17				=	=			+			170		71	0 17930		0	0 12
1M0/04 - 10 01 1411 661 431/01 V					+	+				-	0 23	54 21827	9	0 5506			
Mah pt - 19										ים	[41]	4312	٠				

Table 3 (contd)

Column	Tlesus	Tumoteven	Normal	4400	Turnet - 1e	Turnet cells	Mormal	Fados	033	SEO 95 AA	SEO M AA	SEQ 97 HB	SEO 180 A	6EQ 101 A	SEO 110 A	6EQ 111 AJ	6EQ 112 A	SEQ 114 M
STATESTON	edranal gland - h	10	1		Tullion - 10	TOMOS CAME		Linear	P~	0	520	9317	16583]	5311	3706	929461	560	18327
Company   Comp	hymph noce - h		<del>                                     </del>	<u> </u>		<del> </del>	_		<del></del>					6045	4161	166481	1113	4801
Services   1   1   1   1   1   1   1   1   1	mammary gland - h									121	306	549	403	452	1581	1216	553	3951
Section									<del></del>						4397	15743	11171	11145
Section	cerebellum - h															76914	1399	51344
Company	fetal bran - h									0	1302	3571	20240	4881	7201	58138	1589	26240
STATE   13	precente - h	F							<b></b>							34771	2075	28256 48585
## Company of the com	prostate, h		1	2						583	1511	786	7309	610	3972	14650	1414	30916
Section   1		<del> </del>							<del>                                     </del>						5618	20032	1120	18166
Column	(atal bang - h																1638	97915
Column   C										32	708					41333	1154	37255
## Company	email intestine - h										524					10971	1713	19616
The state of the			2	đ						1080	264	1535	4310	1760	945	16499	1055	6030
The second column   1						<b></b>	-	-										4256
The color of the	lung - h		, z	3														28615
STATE OF THE PROPERTY OF THE P		<del> </del>						-					4231			67389	890	24003
The second   1	thyrmus -h		2	7														13111
The color of the			2	9						581	660	1230	4784	3196	2990	21697	910	24405
Section   Sect						F		30									1555	56590
Section	HMEC		3	2										115	3044	1023	1192	2038
Section   Sect						<del>                                     </del>			-						3409	1110	805	0
September   30	Pencreas - N								=		451						630 946	1325
March   3	Skeletel musicle - h		3	7						0	375	168	. 0		1441	1996	720	0
Color	latel fiver- h	<del> </del>				ļ		-	-						1194	3263	658	901
Company   Comp	thyrnus,h		4	0	F					143	522	0	499	362	2819	541	1219;	0
Section   Column	Felial brain - h	<u> </u>	1	2						629	409	. 0	573	454	1760	377	2223	0
Till agent	Salvary of h													145 3678	1860 Z371		1265	
Column	HT218-normal							=		0	323	0	. 0	0	734	53	348	0
151   152   153	HT213-normal	<del></del>	<u> </u>					<del></del>	<u> </u>	0			18	0	83	2404	165	
Section   Sect	Bev-13						356			4165	5699	345	634	323	8777	296	34191	
Section   Sect	carebellum - h						344			0	254	82	225	35	297	64	\$59	0
Company   Comp	brain -h	$\vdash$	$+ \equiv$					334				32			746	0	1868	- 0
Table   196   19	lymph node - it		<b></b>				337			0	- 0	11	19	. 24	91	45		0
April			<del>                                     </del>					<del> </del>	<del> </del>	1667		0	1912	109	2629	458	1452	
### Annual	HT396-normal						327			9	591		171					9621
1310   2010   1700							321			218	45	0	0	0	0	72	755	0
1346   1312   141   3   1232   145   2523   3   751   151   252   253   3   751   151   253		ļ.——-					320	<del>                                     </del>			1322							2669
Section   Sect	truchae - h		=				316			812	74	. 0	1132	1683	2543	0		
March   Marc		├	<del>                                     </del>				311		<del>                                     </del>					47	58	251		0
Section   Sect	prostate, h						309					47	135					
Table 1							305			0	79		397	200	520	535	749	
Section   1986			-				303	<del></del>				3064				2554	933	
Separt	tests - h						298					2195	2065		4087	1220		4479
Second of the content of the conte							296						807	515	399	881	931	91
Table   Tabl	spinal cord - h						294	<del> </del>	_							75	1715 546	450
Part	ekaletel muecle - h						290			1424	482	0	3317	685	1687	277	901	2243
##ACC   275 275 0 14 67 0 10 497   11 501 0 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1			-			-	279	}	-			0	0	249	1352	374	864	
First Column	HPAEC						275	275							407	181	801	
Section   1	HT392-normal	<del></del>					266				0		161	٥	0	245	738	
First   Firs	Ber 11													599	531	2987	1460 751	- 8
Deck   221   221   0   535   285   217   61   220   234   617   0   0   0   0   0   0   0   0   0	HT372-normal						234			78	1472	0	191	104	1276	0	1532	0
Berr	Bay-7 Bay-6	<del> </del>		_					<del>!</del>			265	217	61	228	2538	817	0
Section	B=v-2						229		=			0	12	25	564	464	719	
Heart.h     2715   0   4666   0   0   0   3214   10   10   10   10   10   10   10	Mackdor - h						222			0	57	0	0	96	549	48	483	O C
Field New	Heart - h		<del></del>			<del></del>		<del></del>	<del></del>					230	741	693	976	<del></del>
### First Company Comp	fatal liver- It						213	=		35	94	147	0	57		162	1042	0
IEFM N TOPB   Contemport Phinse   195	HCAEC						211	211		0	67	0	0	69	0	255	793	
IEFM N TOPB   Contemport Phinse   195	fetal brain - h			$\dashv$											264		751	
IEFM N TOPB   Contemport Phinse   195	Ouodenum - h						205			0	180	92	0	0	? 733	0	765	21
IEFM N TOPB   Contemport Phinse   195			L						$\vdash$				125	0	558	0	725	
IEFM N TOPB   Contemport Phinse   195	mots - h		F	<del>,  </del>			199	<u> </u>	_	95		0	111	149		477	461	
Wi-SS 726	HEPM 3d TGFB1 detargent+DNase						195				99		156	76	239	0	397	- 0
Serge number	Styrmus -It	<b></b>	_						<del></del>					78	366	0	377	
heg. h   59	lymph nade - h						61		=	0	973		0	189	1195	64	939	0
Part	tung - h	<u> </u>					57 57	<u> </u>		0	462	240	142	182	608	62	767	0
Figs. Apr. Col. 1979	heart - h						55		匚			0	279	119	338	0	522	- 0
feet desires	lotal byer- h						51			. 0	0	314	30	45	455	386	326	ŏ
FEELA-D-01199	fetal lociney - h			$\Box$		79	49		<b> </b> -							454	774	276
IEEL-06-071199	HELA-4h-031899					. 61				0	337	0	201	D	698	102	779	
FELLAN-071999   580   294   669   0   448   76   6271   1471   2176   0	HELA-9h-031699	├	<u> </u>					<b>-</b>	<del></del>					. 51	493		646	0
FEEA DISPATISES   97	HELA-68-031899									294	689			76	6211	1347	2176	
HELA-116-311699		L				92			<del></del>		0	0	285	219	285	313	1114	35
NCH-GIZSA	HELA-11N-031699			=		94					126			11				
NCLISC2	NCI+022M			二		146				540	77	240	330	2183	677	42	170	0
SHO-19						148		<del></del> -		275	154		144	1241	0	0	362	
SF-768         156         0         449         289         173         819         836         0         182         0           87-795         156         0         87         0         221         342         0         0         742         499           87-795         158         0         87         0         221         342         0         0         742         499           87-795         159         343         345         175         255         20         253         494         1872           90,4145         162         348         0         0         0         0         239         332         0         284         0           90,4145         162         348         0         0         0         0         239         332         0         284         0	SN8-19					152				0	121	0		553	1020	81		263
SF-795         158         0         87         0         221         342         0         0         742         4919           CCRF-CEM         150         231         343         455         175         255         20         253         464         162           DL145         152         346         0         0         0         229         3521         0         264           DL145         152         346         0         0         0         229         3521         0         264	SNB-75 SF-268	<u> </u>		_+		154 156		$\vdash$ $\dashv$			449	289	173	819	836	0	182	. 0
Duit45 152 246 0 0 0 239 352 0 284 0	SF-296			$\exists$		158			=	0	87							1872
	DU-145					162				346	0	0	0	239	352	0	284	0
	HCT 116									322		344	55	_102	<u> </u>	. 0	198	0

184 Table 3 (cont'd)

				4 161 14064 10 140	EQ 111 A 660 112 A 560 114 M
Tlaste Turner-sym Normel-sym Turner - to Turner - 1 100 100 100 100 100 100 100 100 100		0  377	308] 131	1114) 713	62 j 303 O
160		239 386 0 152	21 45 14 104	4121: 1018 5901: 1078	0 1055 0
7800 T-47D	<del></del>	<del>-       3</del>	150 65	0 336	0 530 0
10		31 447	0 1	123: 541	0 5261 0 236 303 0
LIGHT THE STATE OF		0 203	283 279	1030 237	0 448 0
KB poly A+	<del></del>		131 139	163) 260	O 474 D
HOS poly A*		118 263	01 87	1048 685	0: 553 0
11ACC-62 200		227 691	0 64	1808 1221 167 139	172 257 0
MCF-7/ADR-RES 20	<del></del>	305 524	946 0	73 3428	156 431 0
UTOS (Mandy) poly se	<del></del>	0 0	0 888	293 474	0 197 10 0 858 0
WISH (Collegen) poly A+ 20 458 mesuko mRNA 20		712 1711		369 1345 166 0	0 4521 0
CCL 137 RNA 3/21/86		247 151 0 186		30 115	0 305 0
WI 36 72h 0.5%FBS, 24h 10% FBS		0 0	92 136	41 322	0 477 0
CRC 1441 + 1PA (246) 45.2		0 80		1901 117	104 577 0 0 478: 545
Ken-1 22 Ken-2 23		0 140		01 86	0 4671 0
Kend	<del></del>	-1 6 6	197 155	365 60	0 66 1898
HOP-92		10 0		2918 787	574 294 0 370 870 0
ENCY 24		862 302 2488 529	19 379 0 272	2734 720 5737 330	65, 18 917
19.60		2488 529 27 233		2576 193	0 337 0
NCI-HZI		0 450	847 146	1617 0	0 450 0 0 596 961
RPMI 8226 6 AS49/ATCC 24		Z25 106		637 249 266 923	0 596 961
SD		0 122		3870 467	215 306 270
OVCAR-)	<del>-                                    </del>	18 423	\$4 448	1543 531	362 484 6992
HCT-15		0 84		463 453 62 34	0 196 0
OVCAR4 25		197 270		62 34 8728 1339	0 351 305
OVCAR-5	<del></del>	690 366	992 0	1415 396	452 597 0
SN12C		753 0	0 19	153 245	0 275 0 357 703 0
25		227 541		3188 514 1607 399	189 626 0
igrovi 23		0 212	0 63	47 346	0 204 0
SK-MEL-2		0 572	0 0	624 445	415 653 0 0 453 0
SW MFLS		211 0		1528 325 2049 1651	0 1121 0
SF-539	<del></del>	0 694	1639 0	1332 1027	0 937 5
SK-MEI,-28		92 0	790 267	473 91	32 544 302 0 493 0
UACC-257		406		2108 505 414 119	114 186 0
M14	<del>-+</del>	406 0	0 2572	17839 1425	0 1304 (
MCF7	<del>-    </del>	0 7	0 138	1653 109	0 96 0
HT279		. 0 62t		1375 489	0 800 400 647 221 0
MDA-N 2		0 810		1534 1167	D 1461 1821
179 DOY A*	<del>-     -   -   -   -   -   -   -   -</del>	0 159	187 1711	2315 1851	0 513
KHOS poly A* HTB36 24h YPA RNA 6/23		0 38		37 0	0 404 0
LUCY A CYTH MISSON		605 121		2251 1206	0 1575 : 3066
HTB36 On RNA		0 24	6 0 222	211 117	0 749 (
HT347 456 medullo RNA		359 165	1 0 0	58 1282 3462; 464	0 901 415
3			7 0 0 0 219 657	413 360	0 16 17
HOP-62		663	0 936	12057 4891	0 1033 327
10000000		2021 167	3 53 3315	26597 11907	1155 1018: 316 26 144
3		136 132 363 132	0 0 292	659 229 3005 1672	0 1051 95
PC-3	<del></del>	300 94	5 280 44	1152 492	0 465
ncc-200		307 133	8 0 20	1634 792	0 423
SW-620 HT192		0 23	2 109 0	217 0 822 87	115 396
COLO 205		- 0 50	9 41 8	0 272	0 446
HT218 3		0 126	3 0 56	980 327	150 181 932 725
3		0 47		42 0 273 597	
7.40a		453 205 0 49		54 700	4 1098
HT393	· <del></del>	173 163	0 96	446 195	279 6381 149
RXF 393 TK-10		4314 278		3339: 4922 22112: 4961	102 1376 813 1635 1624 234
Traine 34		1135 439 0 45		327 205	142 545 35
Ma 576T	<del>-   </del>	0 95	1 949 257	17 1399	0 249
		0 50	0 0	2784 1622 0 355	190 439 0 354
MT139 54		0 64		0 355 397 752	0 925
HT155 30	<del></del>	0 25	9 0 47	0 870	
IN 165		402 725		26 1722 41 822	
MT172 62		0 111		0 0	0 552:
HT136	╍╁╾╾┼╼╌┼╾	0 51	18 0 163	59 0	
H11/8		0 15	65 54	270 952	
HT180 66			0 0 364 19 0 179	91 681 7 868	
HT169 - 67 -	╼┼╼╼┼╌	329 42	29 0 77	134 190	169 1029
HT189 66		0	20 66 20	0 61	
HT 190		0 20	59 658 476 50 0 330	27 410 84 1127	0 2057 2
HT145	<del></del>	312 100	50 358 167	701 1787	55 1137 7
HT727 72 72 HT702 73	<del></del>	0 11	0 284	115 2880	
MT314		0	33 0 222 59 0 750	5) 934 100 2499	
HT317 76	╼┼╾╼┼╾		2 0 308	5 446	0 369
Med-Schlastome #425 11/6	<del></del>	0) 8	36 0 466	7 239	
M3127 60			73 260 112	0 560	
HT335			69 0 128 0 289 20	0 215	0 173
HT146 83	<del></del>	- 0 4	50 0 126	51 112	373 1349 1
HT111		221	27 0 0 87 0 52	26 0	
HT398 185		0 to	77 0 105	0 656	0 517
HT 140	<del></del>	0	0 0 53	0 661	0 453
HT172		0 5	81 7 197	0 39X	
TCGP 207		421 6	0 0 45	64 13	67 345
HT 160 216	<del></del>	. 0	0: 0 275	203 40	0; 291
HT307 HT369 224		224 10	68: 173 384	0: 1180 951 400	
HT370 226		0 2	19 0 0	1  90	2 255 720
HT371 226	_++-	0 1	72 0 250	56 20	97 774
KT377 236		0	71 265 69	11 1	25 738 7 298 842
H1362 281		0	39 0 0	0 36 759 79	7 291 642
HT1M 299		0 12	49 620 3a3 33 0 795	0 664	137 802
HTT308 301	<del></del>	570	44 0 280	162 34	0 400
HT392		01	0 0 185	0 12 26 14	
		368	9 0 0	74	174 406
HT312		1 3551	v: 01		
HT312 319 HT162 325	<del></del>	-1 0	0 0 105		100 680
HT312 319 HT162 125 HT185 259		8	0 0 10	14 47	0 6961
HT312 319 HT102 225 HT395 358 HT357 360		0 0 4563 1	0 0 10 69 545 825	14 47 1180 922	0 8961
HT312 319 HT162 125 HT185 259		0 0 4563 1 1843 2	0 0 10	14 47 1180 922 814 874	0 0 896 2 1026 668 1 0 \$757 730 8 4 4457 976 2

WO 00/73469 PCT/US00/14842,

Table 3 (contd)

		Normal-eym	Tumor - 10	Tumor cells	Normal	Endae	p53							SEQ 111 A	SEO 112 A	SEQ 114 M
HIL STRY MCF-7/ADR-RES	155 153							2829 491	517	1977	891	2068 696	12004 10679 25634	10483 5354	665 892 1309	14252 0 2238
MCF7 M14	151						=	5433 3831	1235 0	450	2401	1993	3476 11053	2094 1359 6220	1035	947
UACC-257 UACC-62	147 145	<u> </u>						4023 2545	157	726	756	2137 1215 721	4403	2499 1531	585 805	429 2945
SK-MEL-28 UO-31	143							5634 5324	487	3107	504	442	3098 3000 16384	1020	1536 691	11997 3366
SK-MEL-5 KM-12	142							1336 261	319	0	469	2826 0	3403	2694 379 1717	443	3611
SK-MEL-2 HCT-15	140 139							2614 4852	185 486	655	1930	389	9958	682	979	1620
Malme-3M COLO 205	138 137							1296 3539	101	1993	1664	1417	11150	2354 231	943	2699 1103
LOX IMVI SW-620	136 135							3524 4591	493	1395	1150	826	12216	2457 571	967 850	1756
TK-10 HCT 116	134							4645 1224	318 384	579	1524	323	6640		821 768	
786-0 HCC-2998	132	<del></del>						2284 2684	29	0	1232	719	5639		722	
ACHN PC-3	130 129	<del>                                     </del>						2267 5813	458 370	2068	719	646	13946	2858 2599 (	652 543	. 0
RUF 393 DU-145	126 127		ļ					614 1412	317	5314	911	540	2671	7592 1531	524 666	312
Cate-1 SR	126 125							2183 3471	41		1328	635 330	19003	3126	502 345	1596
A498 RPM 8226	124 123							5481 1951		1125	1967	269	26934	10429	528 563	654
SN12C HL-60	122							2060 930	194	800	178	1633	11740	11038	634 634	937
MOLT-4 DVCAR-5	120							5683 1590	0	1010				753 1900	1205	
K-562 OVCAR-4	118							3767 1258	0	0	850	252	6345	1008	1001 1253	269 657
CCRF-CEM OVCAR-3	116						$\blacksquare$	5623 2090	85	1599	2572	1626	25692	2316 1242	981 552	1345
SF-539 HOP-62	114	<b></b>					F	3527 455	457	10	717	367	16956	693	882 252	1458
SF-295 A549/ATCC	112		<del></del>					2817 1680	539	75	1118	801	17954	1580	941 1074	751
SF-268	110	===				<b> </b>		2259 1264	208	1443	583		11939	4509	643 976	1666
NCI-H5Z2 UZ51 NCI-H460	108						=	2200 2274	209	729	977	739	8651	3516 1892	526 676	2250
SN8-75	106		<b></b>	ļ		<u> </u>		1146	228	. 0	405	289	4322	1334	722 559	0
NCI-H322M SNB-19 NCI-H226	104				=	<u> </u>		2006	316	0	1663	455	4358	2106	812 1091	1908
SK-OV-3	102	===						6105 6603	418	0	1085	615	13274	5271 446	587 380	3219
IGROV1	100	===						212		0	1683	959	10757	0	493	0
OVCAR-8	99 98 97	<u> </u>						3654 2307	0	477	422		7006	376	762 687	481
HOP-92 h fibroblasts 3/31/92 #12	48		<b></b>					334	84	16	260	21	1718	923		
h adult SMC 10/21/92 #17 h kerabnocytes 2/25/92 #10	46							269 534	336		193	62	5234	5718	1436	7982
TCGP AS49 - 1	26						w	1066		0	5421	18	0	353	E25	0
A549 - 4							*	- 0	.0	0	5323	30 49 210	0	587	404	0
A549 - 7		<del> </del>					3	0	0		162	118	10	530	583	0
EKVX - 4							mutent mutent	0	0	0	43690	11	1 0	557	705	a
EKVX - 5							mutent	0			. 0	207	0	283	758	
EKVX - 7 MCF-7 - 1							mutent	0	0	0	718	64		0	621	0
MCF-7 - 4							**	0	0		1155	73	0	353	895	
MCF-7 - 5 MCF-7 - 7							3.5	- 0	0	0	1337	145	0	217	659	
ADR-RES - 1 ADR-RES - 3				<u> </u>			mutent mutent mutent	0	Ö		525	99	0	169	966	
ADR-RES - 5							mutent			! 0	472	112	0	. 0	569	0
ADR-RES - 7 WI 36 - 1							wi		0	1 0	. 0	222		2197		,
WI 38 - 3 WI 38 - 4							**				751	79	1 0	548	548	
WI 38 - 5 WI 38 - 7							**		0		4617		1	0	956	0
HeLa-1 HeLa-3			<u> </u>	<u> </u>			HPV E6	- 8	0	) 0	643	263		74	884	li 0
Hala - 4 Hala - 5						<u>:-</u>	HPV E6		1 0		1166	816		1402	1155	510
Hul.s - 7 H1299 - 1		<u> </u>					mutant		0	)	) 0			0	703	. 9
H1299 - 3 H1299 - 4							mutant mutant		0	0	2070	\$30		147	1242	21
H1299 - 5 H1299 - 7							mutent mutent	- 9	1 0		0			0	719	
A549 - 2 EXVX - 2			<u> </u>				mutent		0		2003	86		0	373	Si
HCT-116 - 1 HCT-116 - 2							w				3756	44		2663	1 516	51
HT29 - 2 SF\$39 - 1							mutani	9						220	659	) (
SF-268-1							wt mutent	- 0			317	2004		1212	595	5
SF-268-2 OVCAR-4 - 1							mutant wt	0	1 0		09	619		375	1271	<u> </u>
OVCAR-1 - 2 OVCAR-5 - 1							mutent				581	154		430	914	1
OVCAR-5 - 2 MCF-7 - 2					F		mutum wi		0	0 0	1433	90		0	632 420	21 5
ADR-RES - 2 Hala - 2						-	HPV E6		0		_0	107		1170	786 760	5
SW480 - 1 SW480 - 2					F	F	mutant mutani		0	0				543	685 879	
H1290 - 2 C33A - 1							mutent	0	0		2573	16	1 6	1147	1143	51 0
C33A - 2					<b> </b>		muturi	0	0	0	1155			114	748	3
U2OS - 1 U2OS - 2					<u> </u>		muterit muterit wr		0	) 0	0	163		1008	871	
Hu68 - 1							¥.				965			646	931	1
WI 36 - 2 Midhail - 1							w			0	265	57		178	636	5
Mikhai - 2 Mikhai - 3								8			696	386		1724	610	1
Mehai - 4 Mehai - 5								0		<u> </u>		75		319	461	1 9
Mithal - 6 Mithal - 8								0		); C	1897	5531		2589	667	
Machinal - 9													7	0	1234	

Table 3 (contd)

		Normal-sym				entre le	12 150	0 95 AA	EQ 96 ANS	SEO 97 H4 S	EQ 100 A 60	0 101 A	EG 110 A	EQ 111 AF6E	112 AISED
issue	Tumor-sym	Normal-sym	Tumor - to 1	umor calls	-	1700		01	91	0					768
P-0.7								0	0			72		2407	364 603
Parg-8		i						0	0	- 0	2910	4771		1191	732
aPang-11							_	- 6		- 6	0	50	0	5703	368
sPero-12				<del> +</del>				0	q	0	11437	102	0	910	636
-Parg-10								- 0	0	- 01	762	80 D	0	206	737
Perg-1					$\rightarrow$		<del></del>	0	81	0	5099	69	0.	337	970
P=9-2 P=9-3		====					-+	- 6	- 8	- 6	3575	67	0	1598	764
							-t	. 0	0	0	217	72	0	1090	1967
laPeng-5					$\overline{}$			0	_ 0	- 0		40	0	59	6221
549 · 8							~	0	0	0	1853	79 207	0:	374	847
XVX · 8							mutant	0	- 01	- 6	0	209	اق	54	5731
CT-116 - 7							<del>-</del>	- 0	- 6	- 0	846	122	0	176	675
CT-116 · 6							muteri	0			3501	- 0	. 0	855	533
T29-1							mutani	01	0	- 0	3147	20	0	214	768
mzs.7		-					mutent	0	0	- 9	467	55		200	654
T29 - 8 F539 - 7							-	- 0	0	- 0	375	252	- 6	21	683
F539 - 0							material	0		- 0	446	164	0	706	829
F-268-7							muteri		- 6	10	0	183	0	203	548
F-268-0							w		0		1305	423	0	0	935
NCAR-4 - 7					-		w	0	0		527	329	9	2772	2164
VCAR-4 - 8							mustant	0	0	9	326	315	0	603 511	550
WCAR-S · 7							muteri	- 0	0	- 8	740	194	0	510	860
ACF-7 - 8							<del></del>	0			3013	o o	0	295	1032
DR-RES - 8					<del></del>		HPV E6	0	0		2243	117	0	139	675
tela-8		<b></b>	ļ				mutent			Q	1081	452		O	1025
W480 - 7	<del></del>				-		muteri	0	0	0	7328	417	- 0	302	712
W480 · 6	<del></del> -	├─┈	F				mutant	0		0	2363		0	163	760
1299 - 6 33A - 7	<del></del>						70.001	0	0	0	1813	- 8	- 6	528	1063
33A · B						-	mutent	0	- 0			_0	0	13!	851
72OS - 7						-	mutant		0	0		167	0:	668	868
70S - 8		<del> </del>	<del> </del>			_	w	0		. 0	4024	909	0	171	578;
te68 - 7	<del></del>	<del>                                     </del>	<del> </del>				w	0	0	01		- 0	0	301	9731
1#68 - 8 N1 38 - 8	<del></del>	t					*	0		- 8	304	1464	1336	1421	1814
S8 medulo RNA						—Т	├──-	· 0	265 104	154	32	01	42	445	338
PL 1572 3/17/89		<u> </u>	<u> </u>			64		274	494	. 0	25	153	872	2372	1229
Der 4		<del></del>	<del> </del>					1326	1327	0		70	5103		922
136T	<del></del>	<del> </del>	<b></b>					20	184	0		65 60	723 4081		1937
HT378	1	1					-	278	2601	0	870 449	- 60	494	95	2033
HT308						<del></del>	├──┼	0		168	34	115	0		63/1
Bev-3		ļ	<b>└</b>			173_	<del></del>	- 9	336		.0	_0	16	101	345;
Bev-5						177	1	576	386		104			119	621
9009	<del></del>	<del>                                     </del>	<del> </del>	-					1129		P	0		1516	999
keratmocytes 2/25/92 #10		†	1			237		0			242	16	463		1306
17B10		·				<u> </u>	$\vdash$	0			91	46			1057(
foroblesta 3/31/92 #12			<del></del>		-		<del></del>	<del></del>			187	- 69	186		1021
prostate, h	<del> </del>		<del> </del>		<del></del>			52		0	492	D46	1535		606
MINING-OS poly A+	<del></del>							1046			572 778	1366	2116 2288		1231
SA-OS (Mundy) poly A*						<u> </u>	<u> </u>	1104				180	0		615
HCT-116 - 3							<del></del>				705	56		1404	189
HCT-116 - 4		4		<del></del>		-	<u> </u>			0	377	14		7541	414
HCT-116 - 5	<del></del>		<del>                                     </del>				w _			0	249	0			915
HCT-116 - 6	<del></del>	<del> </del>	<del>                                     </del>	t — —			wt				4346	100			903
A540 - 6 HT29 - 3	<del>                                     </del>						mutent				3771	100			366
EXVX - 6						<b>↓</b>	mestant				1 51			913	641
HT29 - 4		<del></del>	<del></del>	<u> </u>	₩-	-	mutani				1269	256			711
HTZ9 - 5		+	+	<del></del>			mutant			0	0	154			550
HT29 · 6	<del></del>		-		1		wi					42 93		650	544
OVCAR-4 - 3 OVCAR-4 - 4							3		9 9	9 0	3926	734		977	545
OVCAR-4 - 5					↓	<del> </del>	w _		<del>} - `</del>	<del></del>		903		190	753
OVCAR-4 - 6			<b></b>	<del></del>	<del> </del>	+	W			<del>-</del>	. 0	131		315	662
SF539 - 3		+	<del></del>		+	+	w .		1	0		99		484	524 896
SF539 - 4	<del> </del>	+	+	<del>                                     </del>	_	_	w			9 0			<u> </u>	664	1057
SF539 - 5	+	<del>                                     </del>	<del> </del>				w			0		62		276	968
SF539 - 6 OVCAR-5 - 3				T			mutant			0 0				72	758
OVCAR-5 - 4				<b>↓</b>	+	<del> </del>	mutent	<del> </del>	2	0 0	444	0		0	397
OVCAR-5 - 6		<del> </del>	-	<del> </del>	+	+	muters	<del></del>		0 0	992	175		0	723
ADR-RES - 6	+	+	+	<del> </del>	$\overline{}$	+	wt		0}	0 0		35		543	1131
MCF-7 - 6	+	+	+		1		HPV E6		0	9		963		674	771
HeLe-6 H1290-6	-	1	1				muteri			0 9				366	641
SW480 - 3				+	4—	+	mutant		0	0 0		90		0	706
SW480 - 4			1	+		+	mutent		0			577		379	1149
SW460 - 5		+		<del> </del>	+	+	mutent		0	0 9	240	450	il	1271	1267
SW480 · 6	+	+	<del></del>	<del> </del>	1	<del>                                     </del>	mutani		0	0 5				0 165	521
C33A - 3	+	1		L			mutern		0		211		;	0 661	1143
C33A · 5				1	-	+	muteri	<del></del>	8		675			0 1994	1255
					+	+-	wi				0 0	807		0; 0	616
CTIA - 6				+	+	+	WI TOUR		0	ŏ	85	934	st	0 201	726
He58 - 6					+	1_	metern		0	0 (	2742	15		0 146	681
He56 - 6 U2OS - 3		-	+	1											
He56 - 6 U2OS - 3 U2OS - 4							mutan)			0(	1376	219		0 622	716: 626.
Hu58 - 6 U2OS - 3 U2OS - 4 U2OS - 5						$\vdash$	mutant		0	0 - 0	0 1376 0 528	219		0 1097	626. 7391
He66 - 6 U205 - 3 U205 - 4 U205 - 5 U205 - 5									0	0 0	0 1376 0 528 0 4047 0 4744	215		0 1097; 0 0! 0 7551	626. 7391
Hat58 - 6 1/205 - 3 1/205 - 4 1/205 - 5 1/205 - 5 1/205 - 5 Hat58 - 3						E	emutanti wri		0	0 0	0 1376 0 528 0 4047 0 4744 0 1334	219	0	0 1097; 0 0 7551 0 2592	626. 7391 8061 1018
Hu66 - 6 1/205 - 3 1/205 - 4 1/205 - 5 1/205 - 5 Wi 36 - 6 Hu66 - 3 Hu68 - 4							mutant		0	0 0	0 1376 0 528 0 4047 0 4744 0 1334 0 740	215 204 2364 1264	) 	0 1097; 0 0 0 0 7551 0 2592 0 0	626 . 739 ! 806 ! 1018 :
Net64 - 6 L/203 - 3 L/203 - 4 L/203 - 5 L/203 - 5 W1 36 - 8 Net64 - 4 SF-208-3							mutant ed ed ex mutant mutant		0	0 0 0	0 1376 0 528 0 4047 0 4744 0 1334 0 740 0 6402	215 20 236 126 126	0 0 4 8 4	0 1097; 0 0 0 0 7551 0 2592 0 0 751	626. 7391 8061 1018: 5541 721
Net6 - 6 1/20S - 3 1/20S - 4 1/20S - 5 1/20S - 5 W130 - 6 Net6 - 3 Net6 - 4 SF-280-3 SF-280-4							mutant ed ed ex mutant mutant mutant		0	0 0 0	0 1376 0 528 0 4047 0 4744 0 1334 0 740 0 6402 0 1850	215 20- 236 126- 1366 685	0 0 1 1 8 4 5	0 1097; 0 0 0 0 7551 0 2592 0 0	626 7391 8061 1016 554 721 954 760
Me66 - 6 LPOS - 3 LPOS - 6 LPOS - 6 LPOS - 6 Me36 - 8 Me68 - 3 FF-288-3 FF-288-3 FF-288-4 FF-288-5							mutant ed ed ex mutant mutant		0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 1376 0 528 0 4047 0 4744 0 1334 0 740 0 6402 0 1850	219 200 2366 1266 1266 1366	0 0 4 8 8 4 5 9	0 1097, 0 0 0 0 7551 0 2592 0 0 751	626. 7391 8061 1016 5541 721 954 760 1099
Ne66 - 6 1205 - 3 1205 - 3 1205 - 4 1205 - 6 1205 - 6 1205 - 6 1405 - 3 1466 - 4 5F-200-3 5F-200-4 5F-200-5 5F-200-6							mutant ed ed ex mutant mutant mutant		0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 1376 0 528 0 4047 0 4744 0 1334 0 740 0 6402 0 1850 0 1850	215 20- 236- 126- 136- 136- 136- 136- 136- 136- 136- 13	0 4 8 4 5 9 9	0 1097. 0 0 101 0 7551 0 25921 0 0 751 0 0 00 0 1567 0 1567	626 7391 8061 1018 554 721 954 7601 1099 645
Ned6 - 6 1/205 - 3 1/205 - 3 1/205 - 4 1/205 - 5 1/205 - 5 1/205 - 6 Ned6 - 3 Ned6 - 3 Ned6 - 4 5F-285-3 5F-285-3 5F-285-4							mutant ed ed ex mutant mutant mutant		0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 1376 0 528 0 4047 0 4744 0 1334 0 6402 0 1850 0 1850 0 1850 0 6046 0 6046	215 200 236 125- 1366 683 683 141 151 151 151 151 151 151 151	0 4 5 9 0 7 7	0 1097. 0 0 0 0 755. 0 2592 0 0 750 0 751 0 100 0 1567 0 0 0	626 7391 8061 1010 554 721 954 760 1099 645
Ne68 - 6 LIGOS - 3 LIGOS - 3 LIGOS - 4 LIGOS - 5 LIGOS - 6 NO 36 -							mutant ed ed ex mutant mutant mutant		0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 1376 0 24047 0 4047 0 1334 0 740 0 6402 0 1850 0 1850 0 604 0 1652 0 6040	219 200 2364 1265 1366 1366 1366 1367 1377 1377 1377 1377	0 0 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	0 1097. 0 0 0 0 755. 0 2592. 0 0 75. 0 0 0 0 100. 0 1567. 0 1398. 0 227	626. 739. 806. 1016. 554. 721. 954. 760. 1099. 645. 831. 928.
Nation 6 1/205 - 3 1/205 - 4 1/205 - 4 1/205 - 5 1/205 -							enutant vel vet soutant mutant mutant mutant		0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 1376 0 2528 0 4047 0 4744 0 1334 0 6402 0 1850 0 1850 0 1625 0 6046 0 5040 0 5040	215 20- 236- 126- 136- 136- 136- 14- 15- 16- 17- 17- 18- 19- 19- 19- 19- 19- 19- 19- 19	5 5 5 9 0 0 7 7	0 1097: 0 0 0 0 755: 0 2592! 0 0 755: 0 0 750: 0 0 0 0 0 1567: 0 0 0 1398 0 227 0 2312	626. 7391 8061 1018 5541 721 954 7801 1099 645 6311 9281 741
Net64 - 6 LYOS - 3 LYOS - 4 LYOS - 5 LYOS - 5 LYOS - 6 NY 30 - 6 Net65 - 3 Net65 - 3 Net65 - 3 Net65 - 3 Net65 - 3 Net65 - 3 Net65 - 1							mutant ed ed ex mutant mutant mutant		0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 1376 0 2376 0 4047 0 4047 0 1334 0 740 0 1334 0 740 0 1850 0 1850 0 1850 0 1850 0 1850 0 1525 0 6046 0 60 0 50 0 153	215 206 236 136 136 136 136 136 136 136 1	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 1097. 0 0 0. 0 7551 0 2592 0 0 7551 0 0 751 0 0 1567 0 1298 0 1298 0 227 0 312 0 96	626, 7391 8061 1016; 5541 721 954; 7601 1009 645 8311 9281 7411
Nation   6   1200   5   1   1   1   1   1   1   1   1   1							enutant vel vet soutant mutant mutant mutant		0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 1376 0 528 0 4047 0 4744 0 740 0 740 0 6402 0 1850 0 1850 0 1625 0 6046 0 6040 0 5040 0 6040 0 1625 0 6040	215 202 236 126 126 136 68 1 4 1 7 7 7 7 7 7 7 7 7 9 9 10 10 10 10 10 10 10 10 10 10	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 1097 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	626. 7391 8061 1010 5541 721 954 7701 1099 645 631 741 3431 3431
Net64 - 6 U2OS - 3 U2OS - 4 U2OS - 4 U2OS - 5 U2OS - 6 W1 30 - 6 Net65 - 3 N							enutant vel vet soutant mutant mutant mutant		0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 1376 0 2528 0 4047 0 4744 0 740 0 1334 0 740 0 160 0 1850 0 1850 0 604 0 600 0 600 0 600 0 600 0 600 0 600 0 600	215 226 2366 1256 1256 1366 1366 14 15 16 17 17 17 17 17 17 17 17 17 17 17 17 17	0 0 1 4 4 5 5 5 9 9 0 7 7 7 0 8 6 6 6 5 5 3	0 1097 0 0 0 0 0 7551 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	626, 7391 8061 1016; 5541 721 954 780; 1099 645 631; 343 343 351 601
Hedd - 6 LIGOS - 3 LIGOS - 4 LIGOS - 4 LIGOS - 5 LIGOS - 6 LIGOS - 6 LIGOS - 7 LIGOS -							enutant vel vet soutant mutant mutant mutant		0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 1376 0 528 0 4047 0 4047 0 1334 0 64020 0 64020 0 1850 0 1850 0 65046 0 551 0 501 0 501 0 501 0 501 0 501 0 501	215 206 2366 1266 1266 1366 1367 13	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 1097   1097	626. 7391 8061 9016: 5541 721 954 780: 1099 645 631 9281 741 3431 601 642 906
Nation   6							enutant vel vet soutant mutant mutant mutant		0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 1376 0 2528 0 528 0 4047 0 4047 0 1344 0 7440 0 1850 0 1850 0 1850 0 1629 0 6046 0 750 0 750 0 750 0 750 0 750 0 750 0 750 0 750 0 750 0 750 0 750 0 750	215 205 236 126-1 1	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 1097   1097	626. 7391 6061 1018 5541 721 7801 7804 7804 7801 1099 645 641 9281 7411 3411 3611 6612
Hedd - 6 LIZOS - 3 LIZOS - 4 LIZOS - 4 LIZOS - 4 LIZOS - 5 LIZOS - 6 LIZOS - 6 LIZOS - 7 LIZOS -							enutant vel vet soutant mutant mutant mutant		0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	D 1376 D 5276 D 5276 D 5276 D 5276 D 64047 D 1334 D 6402 D 6402 D 1850 D	215 215 226 236 126 126 136 168 1 68 1 7 71 1 20 1 20	D D D D D D D D D D D D D D D D D D D	0	625. 7391 6061 9010 9050 9050 721 721 721 725 7801 9099 645 9281 9281 9281 941 941 941 941 941 941 941 941 941 94
Ne66 - 6 L/205 - 3 L/205 - 3 L/205 - 4 L/205 - 4 L/205 - 5 L/205 - 6 N/205 -							enutant vel vet soutant mutant mutant mutant		0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	D 1376 D 5278 D 5278 D 5278 D 6474 D 4744 D 1334 D 1334 D 6402 D 6402 D 1850 D 1850 D 1850 D 1850 D 1850 D 1850 D 1672 D 1673 D	2191 2291 2291 2291 2291 2291 2291 2291	5	0 : 1097 : 0097 : 00 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	626. 7391 8061 1018: 5541 721 780: 1099 645 645 7411 9281 7411 9431 951 9561 5601
Hat64 - 6   U2OS - 3   U2OS - 4   U2OS - 3   U2OS - 4   U2OS - 5   U2OS - 6   U2OS - 6   U2OS - 6   U2OS - 7							enutant vel vet soutant mutant mutant mutant		0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	137676   1	2191 2191 2191 2191 2191 2191 2191 2191	5	0	625. 7391 6081 70101 5081 7584 7781 7781 7781 7781 7781 7781 7781 77

WO 00/73469 PCT/US00/14842 <sub>c</sub>

## Table 3 (contd)

Tissue	Tumor-aym		Tumor - 1a	Tumor cells	Normal	Endos	p33	SEQ 116 S
actional gland - h	<b></b>	- 1			<b></b>			834
lymph node - h bone marrow - h		3						922
mammary gland - h		5	ļ				<u> </u>	2601
pencreas - h	<del> </del>			<del></del>		<del>                                     </del>		235
carebalum - h		7						686
prestary gland - h	<del> </del>		<b></b>		<del> </del>			2327 2719
(etal bren - h placanta - h		10						1303
fetal lodney - h	L	11						717 762
prostate, h (etal iver-h		13		<del> </del>		-		537
salvary of - h		14						548
fetal king - h		15	<b> </b>		<del></del>	├		410
skeletat muscle - h heart - h	<del></del>	17						154
email misethe - h		18						514 292
kidney - h epinal cord - h		19					<del>                                     </del>	250
liver - h		21						51
Spleen - h		22						167 456
stomach -h		24						894
Locas - h		25						- 61
trymus -h HPAEC		27	<del></del>			28		33
thyroid gland - h		29						
RPTEC	<del></del>	30	<del> </del>		├	30		168
Faches - h	<del>                                     </del>	32						. 91
uterus - h		33						196
Pencree - h	<del></del>	35	<del> </del> -		-	<del></del> -	<del> </del>	160
lymph node - h		36						176
Skeletzt muscle - h		37	<del></del>	<b></b>	<del></del>			1036
fetei iver- h Haart - h		39						102
Byrnus,h Duodenum - h		40						102
Duodenum - h Fetal brain - h		41	<del> </del>	<del></del>	<del> </del>	_	<del></del>	121 537
Selvery gl h		43					=	140
tests - h		- 44			365	1-	<u> </u>	
HT216-normal					363_			
HT157-normal					361	100		
Berij Berij	<del> </del>	<del> </del>		<u> </u>	356 354	356 354		1292 1237
cerebellum - h	E				344			85
RPTEC		<del> </del>	<del></del>		342	334		
hymph node - h					332			139
In adult SMC 10/21/92 #17					330	<u> </u>		141
Fatel brain - h HT398-resmel				<del> </del>	328	-		65
diyeta.di					326			386
HT149 - normal HEPM 3d untreated	<del> </del>			<del> </del>	321	<del></del>		
Intervie - P					318			149
traches - h					316			203
thyroid gland - h a slivery gl h	<b></b>				311			173
prostate, h					309			68
pitatury gland - h pancreas - h					307			190
mannary gland - h					303			
blader - h					302 298	├—	<del> </del>	307
leate - h					297			60
Spleen - h					296			21
epinal cord - h email intestne - h	<del></del>				294 293			111
ekeletal muscle - h					290			
bone merrow - h					279		<del>                                     </del>	267 136
actremel gland - h HPAEC					275	275		
HT392-resmal					268			
HT382-normal Bare-11	<del> </del>			<del>                                     </del>	266 239	239		33
Bev-6					235	235		223
HT372-normal				<b></b>	234 233	233		356
Bev-7 Bev-6					231	231		46
Ber 2					229	229	<u> </u>	8;
Bev-1 bladder - h	<b>——</b>			<del></del>	227 222	227	<del>                                     </del>	44
Heart - h					215			
stomach -h fetal liver- h				<del></del>	214 213	<del></del>	├	1000
placente - h					212			123
HCAEC					211	211		
fetal brain - h					210			
Duodenum - h					205			267
Sketetal muecie - h Panoreae - h			<u> </u>		203	-	<b>—</b>	
teate - h					199			
Salvary gt h HEPM 3d TGFB1 detargent+DNase					197	-		46
MEPNI 3d TGFB1 detergent+DNase					195	<del> </del>	$\vdash$	
trymus -h WI-38 72h					179			
tympt node - h tung - h	-			-	61 59	<del>                                     </del>	$\vdash$	
kidney - h					57			
heart - h					55 53	$\vdash$	<del></del>	
fetal lung - h fetal liver- h					51			25
fatel keinev - h					49	$\vdash$		l
HELA-2h-031899 HELA-4h-031899				79 81	<b></b>	<del></del>	<del></del>	524
HELA-9h-031899				ន				71
HELA-0h-031899				86		=		674
HELA-6h-031899 HELA-8h-031899				8 8		Ι		151
HELA-101-031899				92				
HELA-11h-031899	-		-	94		<b> </b>	<b></b>	9.
HELA-12N-031699 NCH-0322M				96 146				120
				148				-
NCI+460				150		<u> </u>		66
NCHH522								
NCI-H460 NCI-H522 SN8-19 SN8-75				152 154				
NCHH522 SN8-19 SN8-75 SF-268			-	154 156				137
NCI-H522 \$N8-19 \$N8-75 \$F-268 \$F-295			-	154 156 158				13
NCH4522 \$N8-19 \$N8-75 \$F-268	-			154 156				13

Table 3 (cont'd)

	Tumoraym	Normal-sym	Turnor - 10	Turrer cells N	iormal  Er	idos pi	3 5	EQ 116 S
Ab1				166			_	- 6
60			<del></del>	168			<del></del> -	
47D				171		=		72
ER 1441 RNA 8/30				181	=		-+	169
1T untraded + DNime				183		— <u>t</u>		47
B poly A+ CS poly A+				196		=	丁	
CHEV				196	$\rightarrow$		<del></del>	25 25
ACC-67				200	-+	$=\pm$	ightharpoons	56
CF-7/ADR-RES TOS (Muney) poly as				204		=		
riSH (Collegen) poly A+				206			-+	200
CO mark des mRNA				205 218		-+		
CL 137 RNA 3/71/88 VI-38 72h 0.5%FBS, 24h 10% FBS				219				
PL 1441 + TPA (24h) 8/30				220			$\rightarrow$	247
en-1				221	—+	<del></del>	-	75
en-2				223		_		
(an-4				241				
10P-82 ADLT-4				347		<del></del>		
ocvx				243 244	<del></del>	$\overline{}$	-+	
6.60 ICHH23				245		$\perp$		
PAR 8226				246		$\rightarrow$	-	24
SABATCC				247 240		-		
SR				249		$=$ $\pm$		6
OVCAR-3 4CT-15				250		=	$\rightarrow$	
WCAR-4				251		-+		
0-31				252 253	-	-+		24
DVCAR-5	<del></del>	<del></del>		754				
INIZC				255				
OX MAY		<del></del>		256 257	-		_+	
GROV1		<del> </del>	<del> </del>	258				15
SK-MEL-2 SK-OV-3				259		=	-	
SK-MEL-5				260		-+		
SF-539	<del></del>	<del> </del>	<del> </del>	261 262	-+	+		
SK-MEL-28 K-562	<del> </del>	<del>                                     </del>	<b>—</b>	263				
UACC-257				264	==		<del></del>	
M14			-	265 267			-	
MCF7	<del></del>	<del></del>	<del> </del>	269				10
MCA-MB-435 HT279				270			$\Box$	
MDA-N				271		+		
Y79 poly A+	1		<del></del>	289	<del>                                     </del>			
KHOS poly A* HT836 24h TPA RNA 6/23	<del> </del>			300				14
HELA-EXP-031829				313				
HTB36 ON RNA	I		<del> </del>	323	-		-	
HT347	<del></del> -	<del>                                     </del>	+	324				17
458 medulio RNA NCI-H226		1		336				
HOP-62			<b>—</b> —	337	<del>  </del>		-+	
MDA-MB-231	+	<del></del>	<del>                                     </del>	339		=		
U251 PT cells poly A+	+			340			$\overline{}$	
PC-3				341				
HCC-2996		<b>└</b>	<b></b>	343 345	<del>!</del>	-	_	
SW-620 HT192	<del> </del>	<del>                                     </del>		346		==		14
COLO 205				347	-	$\rightarrow$		
HT218		ļ		348	<del></del>	-		
K0A-12		<del> </del>	+	350				
HT151	<del></del>	1		351				
HT393				352	<del></del>			4
RXF 393	+		<del></del>	353 355	+			3
TK-10 Maine-3M	+	<del></del>		357				2
His 578T				359		-		- 3
HT213	$\Box$		50 52	<del> </del>	1			
HT288		+	54	+				
HT 139 HT 155		+	56					
HTIGS			54	<del>                                     </del>				,
HT170		<del></del>	60 62	+				-
HT172 HT138	+		63					
HT178			64	+	$+\Box$	$\vdash$		
HT154		+	65	+		$\vdash$		
HT180	+-	+	67					Ε,
HT169 HT189			64		=		<u> </u>	<del></del>
HT143		-	69	+		-	$\vdash$	<del></del> -
HT190	+	+	70	<del></del>	<u> </u>			
HT145 HT227	<del>                                     </del>	$\perp =$	72					
HT302		$\perp =$	73	<b>_</b>	+	<b></b> -	<del> </del>	
HT314		+	74	+	+	<del> </del>		
HT317 Med, Roblestome 8425 11/8	<del></del>	+	77					
HTT23			78				<del></del>	
HT327			60	+	+		$\vdash$	-
HT335	<del></del>	+	62 55	+	+			
HT146 HT348	+		87					1
HT311			170	+	4	<b></b>		+
HT396			185	+	+		<del></del>	<del> </del>
HT140	+	+	189	<b>†</b>	1		=	
HT281 HT372	<del></del>	1	191	1				
TCGP			207		+	<del></del>		+
HT 160		+	216	+	+	_	<del> </del>	1
HT307	+-	+	224	1				
HT369 HT370		土二	Z26		$\perp$	=	-	1
HT371			228	+	<del></del>	<del></del>		-
HT377		+	230 236	+	+	<del>                                     </del>	<del></del>	
MT382		+	281	+				
menunbleatoma RNA HT334	$\pm$		299			$ldsymbol{\square}$	-	
HT338			301	+	<del></del>	+	├~	+
HT392		+	315	+	+	<del>                                     </del>	$t^-$	$\pm -$
HT394	+	+	319					
	<del></del> -	<del> </del>	325			$\sqsubseteq$		+
HT312					1			
HT162			358					
HT162			360	-	==		$\vdash$	+
HT162 HT195 HT157 T-470	163				=			=
HT162 HT295 HT157	163 161 159							

# Table 3 (contd)

Tissue	Tumor-sym	Normal-sym	Tumor - 10	Tumar cells	Normal	Endos	p\$3	5EQ 116 S
H= STRT MCF-TIADR-RES	151 153							0
MCF7	151				$\vdash$			0
M14 UACC-257	147							z
UACC-62 SK-MEL-28	145		<del> </del>		<b>├</b>			3
0031	143							
SK-MEL-5 KM-12	142	<u> </u>	<u> </u>				$\vdash$	91
SK-MEL-2	140							263
HCT-15 Maime-3M	139	<u> </u>	<del></del>					326
COL0 205	137							250
LOX IMVI SW-620	135		<del></del>					-
TK-10	134							
HCT 116 786-0	132							52
MCC-2998 ACHN	131	<b> </b>						76 276
PC-3	129							
RXF 393 DU-145	128		-		<del>                                     </del>			335
Cath-1	126							276
SR A498	125							137
RPM 8226	123 122							120
SN12C HL-60	121							
MOLT-4	120	<b></b>					├	118
OVCAR-5 K-562	118							36
OVCAR-4 CCRF-CEM	117	<del> </del>	<u> </u>	<del></del>	<del> </del>	<u> </u>		642 886
OVCAR-3	115							161
SF-639 HOP-62	113		<u> </u>				世-	
SF-295	112					<b>-</b>		161
A54WATCC SF-268	110			<b></b>				133
NCI-HS22	109		-	<del></del>	<del>                                     </del>	<del>                                     </del>	<del>                                     </del>	204
U251 NCI-H460	107							
SNB-75 NCI-H322M	105		L				<u> </u>	434
SN8-19	104 103	F			$\vdash$			76
NCHHZ26 SK-OV-3	102							1 6
NCH1Z3	101	-	<del></del>	-	<del></del>			77
IGROV1 EKVX	99							) 54
OVCAR-8 MOP-92	98		<del>                                     </del>					4:
h fibroblesta 3/31/92 #12	48							144
h aduk SMC 10/21/92 #17 h karatnocytes 2/25/92 #10	47	<del></del>			$\vdash$			210
TCGP	26						*	
A549 - 1 A549 - 3							w	375
A549 - 4 A549 - 5						-	wi wi	454
A549 - 7							w	34) 7
EXVX - 4							mutani	290
EKVX · 3							mutent	48
EKVX - 5 EKVX - 7							mutent	677
MCF-7 - 1 MCF-7 - 3							w	569
MCF-7 - 4							wt	315
MCF-7 - 5 MCF-7 - 7							wt	
ADR-RES - 1							mutuni	3045 154
ADR-RES - 1 ADR-RES - 4							muten!	71
ADR-RES - 5 ADR-RES - 7	ļ	<b> </b>			-	<u> </u>	mutant mutant	11 94
WI 38 - 1							wt	3
WI 38 - 3	<del></del>				<u> </u>	<u> </u>	wi	28. 56
WI 38 - 5							wt	56
WI 35 - 7 Hata - 1							HPV E6	I (
Hels-3						H	HPV E6	5
HeLs-4 HeLs-5				1			HPV E6	30
HeLa-7						_	- V CO	10
IMD259 - 1							HPV E6	
H1299 - 1 H1299 - 3							MPV E6	
							MULLANI MULLANI MULLANI MULLANI MULLANI	
H1299 - 3 H1299 - 4 H1290 - 5 H1290 - 7							mutant mutant mutant mutant mutant mutant	
141299 - 3 141299 - 4 141299 - 5 141299 - 7 A5499 - 2 EKOX - 2							mutant mutant mutant mutant mutant wit mutant wit	19
H1299 - 3 H1299 - 4 H1299 - 5 H1290 - 7 A549 - 2 EKVX - 2 HCT-116 - 1							HPV E6 mutant mutant mutant mutant mutant wt mutant	192
H1299 - 3 H1299 - 4 H1290 - 5 H1290 - 7 A549 - 2 EKVX - 2 HCT-116 - 1 HCT-116 - 1 HCT-116 - 2							mutant mutant mutant mutant mutant wit mutant wit	193
H1299 - 3 H1299 - 4 H1299 - 5 H1299 - 5 H1299 - 7 A549 - 2 EKVX - 2 HCT-116 - 1 HCT-116 - 1 HCT-116 - 2 SFSS9 - 1 SFSS9 - 7							HEPVES  mutant  mutant  mutant  mutant  wi  mutant  wi  mutant  wi  mutant  wi  mutant  wi  mutant  wi  mutant  wi  mutant  wi  mutant  wi  mutant  wi  mutant  wi  mutant  wi  mutant  wi  mutant  wi  mutant  wi  mutant  wi  mutant  wi  mutant  wi  mutant  wi  mutant	193
H1299 - 3   H1299 - 4   H1290 - 5   H1290 - 5   H1290 - 7   A540 - 2   EVA - 2   EVA - 2   EVA - 2   EVET - 11 							HEPVES  mutani mutani mutani mutani mutani wi mutani wi mutani wi mutani wi mutani wi mutani wi mutani wi mutani wi mutani wi mutani wi mutani wi mutani wi mutani wi mutani	192 62 63
H1299 - 3 H1299 - 4 H1299 - 5 H1299 - 5 H1299 - 7 ABOV. 2 HBCT-116 - 1 HBCT-116 - 1 HBCT-116 - 2 HTC3 - 2 FF490 - 1 SF490 - 1 SF490 - 2 SF490 - 2							HPV 66 muteri muteri muteri muteri muteri muteri wi muteri wi muteri wi muteri wi muteri wi muteri wi muteri wi muteri wi muteri wi muteri wi wi muteri wi wi muteri wi wi	193 523 64 200 63
M1299 - 3 M1299 - 4 M1290 - 5 M1290 - 5 M1290 - 7 A549 - 2 EV/X - 2 MCT-116 - 1 MCT-116 - 2 MT29 - 2 SF-564 - 5 SF-564 -							HPV 66 mulani mulani mulani mulani mulani mulani wi wi mulani wi mulani wi mulani wi wi mulani wi wi mulani wi mulani wi wi mulani wi wi wi wi wi wi wi wi wi wi wi wi wi	19 52 6 20 63
H1299 - 3 H1299 - 4 H1290 - 5 H1290 - 5 H1290 - 7 A549 - 2 EV/X - 2 HCT-116 - 1 HCT-116 - 2 HT-20 - 1 SF-30 - 1 SF-30 - 2 GV/XR - 1 OV/CAR - 1 OV/CAR - 2 OV/CAR - 2 OV/CAR - 2 OV/CAR - 2 OV/CAR - 2 OV/CAR - 2							HPV E6 mulani mulani mulani mulani mulani mulani wi mulani wi mulani wi mulani wi mulani wi wi mulani wi wi mulani wi mulani mulani mulani mulani mulani mulani mulani mulani mulani mulani mulani mulani mulani mulani mulani mulani mulani	192 522 63 53 522 200
H1289 - 3 H1289 - 4 H1289 - 5 H1289 - 5 H1289 - 7 A541 - 2 EVECTIO - 1 HCT-116 - 2 HTT3 - 2 SF50 - 1 SF50 - 1 S							HPV 66 mulani mulani mulani mulani mulani mulani wi mulani wi mulani wi mulani wi mulani wi mulani wi mulani wi mulani wi mulani wi mulani wi mulani wi wi mulani wi wi wi wi wi wi wi wi wi wi wi wi wi	193 520 63 63 52 200 63 63
H1299 - 3 H1299 - 4 H1299 - 5 H1299 - 5 H1299 - 7 A549 - 2 EVVX 3 EVVX 3 HVC1149 - 2 HVC1149 - 2 HVC2 - 3 SF409 - 1 SF409 - 1 SF409 - 1 SF409 - 2 SF409							HPV E6 IMALIAN	19 52 6 30 52 20 8 8 22 177
H1299 - 3 H1299 - 4 H1290 - 5 H1290 - 5 H1290 - 7 A549 - 2 EV/X - 2 HCT-116 - 1 HCT-116 - 1 HCT-116 - 2 HT29 - 2 SF430 - 1 SF430 - 1 SF430 - 1 OVCAR4 - 1 OVCAR4 - 1 OVCAR5 - 1 MCP - 2 ADR-12 MCP - 2 MCP - 2							HPPY E6 IMAGENI IMAGEN	520 520 530 532 532 532 532 532 532 532 532 532 532
H1299 - 3 H1299 - 4 H1299 - 5 H1299 - 5 H1299 - 5 H1299 - 7 A540X - 2 H274 - 1 H274							HOPVES  INVENT  INVENT  INVENT  INV  INV  INV  INV  INV  INV  INV  I	12 622 6 6 33 527 20 20 21 21 17
H1299 - 3 H1299 - 4 H1299 - 4 H1299 - 5 H1299 - 5 H1299 - 7 A549 - 2 EVVA -							HOPV ES INVARIANT INVARIANT INVARIANT INVA INVARIANT INVA INVA INVARIANT INVA INVARIANT INVA INVARIANT INVA INVARIANT INVARIAN	19 822 6 6 20 93 22 20 8 8 8 17 17
H1299 - 3 H1290 - 4 H1290 - 4 H1290 - 5 H1290 - 5 H1290 - 7 A540 - 2 EV/X - 2 EV/X - 2 EV/X - 2 EV/X - 2 EV/X - 2 EV/X - 2 EV/X - 2 EV/X - 2 EV/X - 2 EV/X - 2 EV/X - 2 EV/X - 2 EV/X - 2 EV/X - 2 EV/X - 2 EV/X - 2 EV/X - 2 EV/X - 3 EV/X - 2 EV/X - 3 EV/X -							HOPV ES INCLUME INCLUM	19 82 6 20 63 3 52 20 20 17 19 100
H1299 - 3 H1299 - 4 H1299 - 4 H1299 - 5 H1299 - 5 H1299 - 7 A549 - 2 SF599 - 1 SF599 - 1 SF599 - 2 SF599 -							HOPV ES  mulani mulani mulani mulani mulani mulani mulani wi mulani wi wi wi wi wi wi wi wi wi mulani wi wi mulani wi mulani mul	520 633 520 633 522 200 83 82 222 177 100
H1299 - 3 H1299 - 4 H1290 - 4 H1290 - 5 H1290 - 5 H1290 - 7 A541 - 2 EVY 3 EVY							INDIVES INVARIANT INVARIANT INVARIANT INVARIANT INVA INVA INVA INVA INVA INVA INVA INVA	19 6 6 20 63 22 20 11 11 19 100 27 55 22 22 22 22 23 24 25 25 25 25 25 25 25 25 25 25 25 25 25
H1299 - 3 H1299 - 4 H1290 - 5 H1290 - 5 H1290 - 5 H1290 - 5 H1290 - 7 A560							HOPV ES  mulani mulani mulani mulani mulani mulani mulani wi mulani wi wi wi wi wi wi wi wi wi mulani wi wi mulani wi mulani mul	19
H1299 - 3 H1299 - 4 H1290 - 5 H1290 - 5 H1290 - 5 H1290 - 5 H1290 - 7 A560							INDIVES INVARIANT INVARIANT INVARIANT INVARIANT INVA INVA INVA INVA INVA INVA INVA INVA	199 822 6 6 93 93 20 20 20 20 20 20 20 20 20 20
H1299 - 3 H1299 - 4 H1290 - 4 H1290 - 5 H1290 - 5 H1290 - 5 H1290 - 7 A540 - 2 EVYA - 2 EVYA - 2 HCC119 - 2 HCC119 - 2 HCC119 - 2 HCC119 - 2 FF00 - 1 SF400							INDIVES INVARIANT INVARIANT INVARIANT INVARIANT INVA INVA INVA INVA INVA INVA INVA INVA	199 822 6 6 30 30 20 20 20 21 19 19 19 22 23 24 25 25 26 27 27 27 27 27 27 27 27 27 27
H1299 - 3 H1290 - 4 H1290 - 4 H1290 - 5 H1290 - 5 H1290 - 5 H1290 - 7 A549 - 2 EVYA							INDIVES INVARIANT INVARIANT INVARIANT INVARIANT INVA INVA INVA INVA INVA INVA INVA INVA	199 6 200 532 200 532 200 100 100 27 27 27 27 27 27 27 27 27 27 27 27 27
H1299 - 3 H1290 - 3 H1290 - 4 H1290 - 5 H1290 - 5 H1290 - 5 H1290 - 7 A560 - 2 SF500 - 1 SF500 - 1 SF500 - 1 SF500 - 2 SF500 - 2 SF500 - 2 SF500 - 2 SF500 - 2 SF500 - 2 SF500 - 2 SF500 - 2 SF500 - 2 SF500 - 2 SF500 - 3 SF500 -							INDIVES INVARIANT INVARIANT INVARIANT INVARIANT INVA INVA INVA INVA INVA INVA INVA INVA	199 6 6 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7

190 Table 3 (contd)

	Tumor-sym M	orm al-aym	Yumor - 10	umor cells	Normal	Endos	p33	SEQ 116 S
eng-2								1582
Percel								603
Peng-9 Peng-11		-					-	2503 518
Parg-12								368
P-re-10	==							474
<del>-Parg-1</del>								
2	$\overline{}$							222
sharq-1								
Perg-5								
Pe06							musterii.	- 4
549 - 8 KVX - 8						-	-M	1
CT-116 · 7							w	
CT-116 - 8							muturit	310
129 - 1					_	<b>└</b>	mutant	- 6
1729 - 7 1729 - 8						<del>├</del>	musent	15
F539 · 7						<del>-</del>	-M	25/
F539 · 6							mutant	211
F-268-7						<b>⊢</b> −	mutant	50. 40
F-268-6 WCAR-4 - 7					├		wi	
WCAR-4 - 8					$\vdash$	1	muteri	63
VCAR-5 - 7							mutant	10
WCAR-5 - 8						<b>↓</b>	mutent	85
108-RES - 8						+	HPV E6	
44.0			<del></del>			+	mutent	
SW480 - 7	<b>⊢</b>		<del></del>			=	muteri	
W480 - 6	<del>├</del> ───					+	muturit	
41299 - 8 2334 - 7						+	mutent	
33A - 8			<del></del>	<del></del>		1	mutent	72
J2OS - 7	<b>├</b>		<del> </del>			$\mathbf{I}$	mutant	1
J203 - B	<del> </del>					1	w	-
466 · 7			$\Box$		<del></del>	+-	wi	<u> </u>
Ha66 - 6 W1 38 - 6	$\Box$		<del> </del>	+	+-	+-	1	
458 medulio RNA	<b>├</b>		<del></del>	<del> </del>				
CRL1672 3/17/89	<del></del>						4	2
Bev-4					<del></del>	-	+	1
HT368			<del> </del>	<del></del>	+-	+	<del>                                     </del>	
HT385	I				<del></del>	1		
HT308			<del> </del>			173	_	+
Ber 5	<del></del>					175	+-	+ +
Resid			1	<del>                                     </del>	┼──	+"	+-	1
h kerstnorytes 2/25/92 #10				<del> </del>	+	237		
10 عجا	+							
HTB10 N Stroblesta 3/31/92 #12	+					┿~		
prostate h				<del></del>	+	+		
MNNG-OS poly A+			+	<del> </del>				
SA-OS (Mundy) poly A+	<del></del>							
HCT-116 - 3			-	<b></b>	+	-	-	<del> </del>
HCT-116 - 4			+-		+	+	- W	<b>—</b>
HCT-116 - 5	<del> </del>		+	<del></del>		1	wt	
HCT-118 - 6	+						w	
A549 - 6 HT29 - 3						+	mutani	
BKVX - 6	$\Box$		+		+	+-	mutant	
HT29 - 4			<del> </del>	<del> </del>	_		mutan	
HT29 - 5	+		+				mutani	
HT29 - 6 OVCAR-4 - 3	<del>+</del>			-	+		- # -	
OVCAR-4 - 4						+-	-155	_
OVCAR-4 - 5		<del> </del>		+	+	_	wi	
OVCAR-4 - 6	+		<del> </del>	<del> </del>			wt	
SF539 · 3							w	
SF539 - 4 SF539 - 5			Ţ		+		w	
SF539 · 6	$\perp$		+	+	+-	$\pm$	mutan	. 2
OVCAR-5 - 3		<del></del>	+	$\vdash$			mular	•
OVCAR-5 - 4	+				$\bot$	4	muter	:
OVCAR-5 - 6 ADR-RES - 6						$\dashv$	menter w(	-
MCF-7 - 6			+	<del></del>		+-	HPV	6
HeLe - 6		+	+		ᆂᆖ		muter	n [
H1299 - 6	+	<del></del>			$\perp$		muter	ıt .
SW480 - 3 SW480 - 4					+		mutar	<del>1</del>
SW480 - 5		<del></del>	+	<del> </del>	+-	$\dashv$	muter	<u> </u>
SW480 - 6		+	<del></del> -		ユニ		mute	x
C33A - 3	<del></del>				$\perp$		muter	vt .
CISA - 4	1					+	muta	<del>:  </del>
C334 - 6			<del></del>	+	+-	$\overline{}$	- COLUMN	1.
He68 - 6	4	<del> </del>	+	<del></del>		$\pm$	mute	u
U205 - 3	+	<del> </del>				<b></b>	muse	ut
U2OS - 4 U2OS - 5					<del>                                     </del>	+-	mute	7
U2OS - 6				<del></del>	+-	+	W.	
WI 38 - 6		+	<del></del>	+			wt	
Issues 1		<b>—</b>				$\blacksquare$	wt	_
7.00	<del></del>			$\perp$		—	muta	<u> </u>
H468 - 4			<b>—</b>				mute	nd 1
SF-268-3			+	+		$\bot$	mute	Μ
SF-268-3 SF-268-4 SF-268-5		<del> </del>				$\perp$	$\neg \neg$	
SF-268-3 SF-268-4 SF-268-5 SF-268-6		<del> </del>	+					
\$F-268-3 \$F-268-4 \$F-268-5 \$F-268-6 DuParg-13			+==				_	
5F-268-4 SF-268-5 SF-268-5 SF-268-6 Outpurg-13 Middel - 20					=	#	==	_
SF-269-3 SF-269-5 SF-269-5 SF-269-5 DiPring-13 Mithal - 20 Mithal - 21						丰	-	ni -
\$F.200-1 \$F.200-1 \$F.700-5 \$F.700-5 \$F.700-5 \$P.700-1 \$P.						Ŧ	muta	m l
\$F-208-1 \$F-208-4 \$F-208-6 \$F-208-6 \$F-208-6 \$P-							muta	nt .
\$F-289-3 \$F-289-4 \$F-289-5 \$F-289-5 \$F-289-6 DePerg-13 selected - 20 labeled - 21 Lebeled - 22 OVCARS - 5 Million - 10 Million - 10 Million - 11							muta	rd .
5F-200-3 5F-200-4 5F-200-5 5F-200-5 5F-200-6 0xProp-13 without - 20 Without - 20 Without - 21 Without - 22 OVCAR-6 - 5 Without - 10 Mittout - 11 Mittout - 11 Mittout - 11 Mittout - 12							muta	ni .
\$F.200-3 \$F.200-4 \$F.200-4 \$F.200-4 \$F.200-6 \$F.200							muta	ni .
\$F.200-3 \$F.200-4 \$F.200-4 \$F.200-5 \$F.200							muta	ni
\$F.200-3 \$F.200-4 \$F.200-4 \$F.200-4 \$F.200-6 \$F.200							muta	rd .

4	
<u>o</u>	
5	
æ	

Gene Name	SP	O# na	SP ID# na ID# aa	Family	Group	Length_AA	Extra-Catalytic Domains (Amino acid positions)
X69117 h beta adrene	Ξ	-	122	AGC	GRK	688	Regulator of G protein signaling domain 54-175, PH domain 559-652.
AA144574 m	Σ	7	123	AGC	GRK	378	PH domain 249-337
AA210825 h	: I	6	33	AGC	PKC	978	Phorbol esters/diacy/glycerol binding domain (C1 domain) 239-287; PH domain 497-577
AA316804 h	Ŧ	=	132	AGC	PKC	890	Phorbol esters/diacy/glycerol binding domain (C1 domain) 155-204 and 272-321; PH domain 417-532
AA887783 h	I	~	142	AGC	SGK	446	PX domain 13-120
AA021445 h 3	Ξ	33	152	CAMK	EMK	1311	Vitamin K-dependent carboxylation/gamma-carboxyglutamic (GLA) domain 1072-1113
R31237 1 h, AAC3348	I	×	55	CAMK	EMK	729	UBA domain 327-365
406786.5 h	Ξ	ဗ္တ	156	CAMK	EMK	1330	PAS domain 133-186, 247-280, 354-386
Z36720 h	I	4	161	CAMK	MLCK	874	WD domain, G-beta repeat 674-711
SGK088 h	Ι	45	162	CAMK	Trio	. 2287	Immunoglobulin domain 1-62, 97-153, 221-277, 518-578, 1617-1678; Fibronectin type III domain 301-390, 1697-1779
R19772 h	Ι	4	164	CAMK	Trio	1287	RhoGEF domain 235-405; Fibronectin type III domain 870-955; Immunoglobulin domain 786-951; PH domain419-528
17000139801197 h, IR	¥	92	195	Other	IRAK	596	Death domain 26-106
AA088547 h	I	8	197	Other	IRE	922	PQQ enzyme repeal 39-76
AA232253 h	I	82	201	Other	MLK	800	SAM domain (Sterile alpha motif) 337-408
AA599286 h	Ι	8	808	Other	SLOB	649	PX domain 16-122
AA836348 h	I	113	232	STE	NEK	836	Regulator of chromosome condensation (RCC1) 387-427, 427-480, 483-532, 598-650
PAK6 h	Ξ	115	234	STE	STE20-02	719	P21-Rho-binding domain 11-69

#### FIGURE 1A

[ID NO: 122\_X69117\_H BARK2\_H
EAVLADVSYLMAMEKSKATPAARASKRIVLPEPSIRSVMQKYLAERNEITFDKIFN
FLLFKDFCLNEINEAVPQVKFYEEIKEYEKLDNEEDRLCRSRQIYDAYIMKELLSC
.\*FSKQAVEHVQSHLSKKQVTSTLFQPYIEEICESLRGDIFQKFMESDKFTRFCQWKNV
!LNIHLTMNEFSVHRIIGRGGFGEVYGCRKADTGKMYAMKCLDKKRIKMKQGETLALNER
IMLSLVSTGDCPFIVCMTYAFHTPDKLCFILDLMNGGDLHYHLSQHGVFSEKEMRFYATE
IILGLEHVHNRFVVYRDLKPANILLDEHGHARISDLGLACDFSKKKPHASVGTHGYMAPE
VLQKGTAYDSSADWFSLGCMLFKLLRGHSPFRQHKTKDKHEIDRMTLTVNVELPDTFSPE
LKSLLEGLLQRDVSKRLGCHGGGSQEVKEHSFFKGVDWQHVYLQKYPPPLIPPRGEVNAA
DAFDIGSFDEEDTKGIKLLDCDQELYKNFPLVISERWQQEVTETVYEAVNADTDKIEARK
RAKNKQLGHEEDYALGKDCIMHGYMLKLGNPFLTQWQRRYFYLFPNRLEWRGEGESRQNL
LTMEQILSVEETQIKDKKCILFRIKGGKQFVLQCESDPEFVQWKKELNETFKEAQRLLRR
APKFLNKPRSGTVELPKPSLCHRNSNGL

SEQ ID NO: 123\_AA144574\_M BARK2\_M
CFVVYRDLKPANILLDEYGHVRISDLGLACDFSKKKPHASVGTHGYMAPEVLQKGTCYDS
SADWFSLGCMLFKLLRGHSPFRQHKTKDKHEIDRMTLTVNVQLPDAFSPELRSLLEGLLQ
RDVSQRLGCGGGGARELKEHIFFKGIDWQHVYLRKYPPPLIPPRGEVNAADAFDIGSFDE
EDTKGIKLLDCDQDLYKNFPLVISERWQQEVVETIYDAVNADTDKIEARKKAKNKQLGQE
EDYAMGKDCIMHGYMLKLGNPFLTQWQRRYFYLFPNRLEWRGEGESRQSLLTMEQIMSVE
ETQIKDRKCILLRIKGGKQFVLQCESDPEFAQWLKELTCTFNEAQRLLRRAPKFLNKPRA
AILEFSKPPLCHRNSSGL

SEQ ID NO: 124\_AA826850\_H
MGSSMSAATARRPVFDDKEDVNFDHFQILRAIGKGSFGKVCIVQKRDTEKMYAMKYMNKQ
QCIERDEVRNVFRELEILQEIEHVFLVNLWYSFQDEEDMFMVVDLLLGGDLRYHLQQNVQ
FSEDTVRLYICEMALALDYLRGQHIIHRDVKPDNILLDERGHAHLTDFNIATIIKDGERA
TALAGTKPYMAPEIFXSFVNGGTGYSFEVDWWSVGVMAYELLRGWRPYDIHSSNAVESLV
QLFSTVSVQYVPTWSKEMVALLRKLLTVNPEHRLSSLQDVQAAPALAGVLWDHLSEKRVE
PGFVPNKGRLHCDPTFELEEMILESRPLHKKKKRLAKNKSRDNSRDSSQSENDYLQDCLD
AIQQDFVIFNREKLKRSQDLPREPLPAPESRDAAEPVEDEAERSALPMCGPICPSAGSG

SEQ ID NO: 125\_AA960957\_H
MGGNHSHKPPVFDENEEVNFDHFQILRAIGKGSFGKVCIVQKRDTKKMYAMKYMNKQKCI
ERDEVRNVFRELQIMQGLEHPFLVNLWYSFQDEEDMFMVVDLLLGGDLRYHLQQNVHFTE
GTVKLYICELALALEYLQRYHIIHRDIKPDNILLDEHGHVHITDFNIATVVKGAERASSM
AGTKPYMAPEVFQVYMDRGPGYSYPVDWWSLGITAYELLRGWRPYEIHSVTPIDEILNMF
KVERVHYSSTWCKGMVALLRKLLTKDPESRVSSLHDIQSVPYLADMNWDAVFKKALMPGF
VPNKGRLNCDPTFELEEMILESKPLHKKKKRLAKNRSRDGTKDSCPLNGHLQHCLETVRE
EFIIFNREKLRRQQGQGSQLLDTDSRGGGQAQSKLQDGCNNNLLTHTCTRGCSS

SEQ ID NO: 126\_TBK1\_H

MQSTSNHLWLLSDILGQGATANVFRGRHKKTGDLFAIKVFNNISFLRPVDVQMREFEVLK

KLNHKNIVKLFAIEEETTTRHKVLIMEFCPCGSLYTVLEEPSNAYGLPESEFLIVLRDVV

GGMNHLRENGIVHRDIKPGNIMRVIGEDGQSVYKLTDFGAARELEDDEQFVSLYGTEEYL

HPDMYERAVLRKDHQKKYGATVDLWSIGVTFYHAATGSLPFRPFEGPRRNKEVMYKIITG

KPSGAISGVQKAENGPIDWSGDMPVSCSLSRGLQVLLTPVLANILEADQEKCWGFDQFFA

ETSDILHRMVIHVFSLQQMTAHKIYIHSYNTATIFHELVYKQTKIISSNQELIYEGRRLV

LEPGRLAQHFPKTTEENPIFVVSREPLNTIGLIYEKISLPKVHPRYDLDGDASMAKAITG

VVCYACRIASTLLLYQELMRKGIRWLIELIKDDYNETVHKKTEVVITLDFCIRNIEKTVK

## FIGURE 1B

VYEKLMKINLEAAELGEISDIHTKLLRLSSSQGTIETSLQDIDSRLSPGGSLGTHPKDRNVEKLQVLLNCMTEIYYQFKKDKAERRLAYNEEQIHKFDKQKLYYHGTDECVKKYEAFLNKSEEWIRKMLHLRKQLLSLTNQCFDIEEEVSKYQEYTNELKMFTASSGIKHTMTPIYPSSNTLVEMTLGMKKLKEEMEGVVKELAENNHILERFKGGLRNVDCL

SEQ ID NO: 127\_AA305176\_H
MDPTAGSKKEPGGGAATEEGVNRIAVPKPPSIEEFSIVKPISRGAFGKVYLGQKGGKI
VKVVKKADMINKNMTHQVQAERDALALSKSPFIVHLYYSLQSANNVYLVMEYLIGGDV
LLHIYGYFDEEMAVKYISEVALALDYLHRHGIIHRDLKPDNMLISNEGHIKLTDFGLS
TLNRDINMMDILTTPSMAKPRQDYSRTPGQVLSLISSLGFNTPIAEKNQDPANILSAC.
ETSQLSQGLVCPMSVDQKDTTPYSSKLLKSCLETVASNPGMPVKCLTSNLLQSRKRLA'
SASSQSHTFISSVESECHSSPKWEKDCQV

SEQ ID NO: 128\_AA116841\_M TRPIPWPEGEEKLSDNAQSAMDMLLTIDDSKRAGMRELKQHPLFSEVDWENLQHQTMP1 POPDDETDTSYFEARNNAQHLTVSGFSL

SEQ ID NO: 129\_AA256100\_H
MAMTAGTTTTFPMSNHTRERVTVAKLTLENFYSNLILQHEERETRQKKLEVAMEEEGLAD
EEKKLRRSQHARKETEFLRLKRTRLGLDDFESLKVIGRGAFGEVRLVQKKDTGHIYAMKI
LRKSDMLEKEQVAHIRAERDILVEADGAWVVKMFYSFQDKRNLYLIMEFLPGGDMMTLLM
KKDTLTEEETQFYISETVLAIDAIHQLGFIHRDIKPDNLLLDAKGHVKLSDFGLCTGLKK
AHRTEFYRNLTHNPPSDFSFQNMNSKRKAETWKKNRRQLAYSTVGTPDYIAPEVFMQTGY
NKLCDWWSLGVIMYEMLIGYPPFCSETPQETYRKVMNWKETLVFPPEVPISEKAKDLILR
FCIDSENRIGNSGVEEIKGHPFFEGVDWEHIRERPAAIPIEIKSIDDTSNFDDFPESDIL
QPVPNTTEPDYKSKDWVFLNYTYKRFEGLTQRGSIPTYMKAGKL

SEQ ID NO: 130 AA210825 H DSLLPTPALGTPLPTPWPVGSLRTPLSLESTRSPTQRLLPSTPKDPAILRSPPPARSFLG SPLSHHLLTRSRGSRTQGPPGPPGGSRVGSRRAVPGLPPWPPPPHYPAGLPGSPGPGSPP PPGGLELQSPPPLLPQIPAPGSGVSFHIQIGLTREFVLLPAASELAHVKQLACSIVDQKF PECGFYGLYDKILLFKHDPTSANLLQLVRSSGDIQEGDLVEVVLSASATFEDFQIRPHAL TVHSYRAPAFCDHCGEMLFGLVRQGLKCDGCGLNYHKRCAFSIPNNCSGARKRRLSSTSL ASGHSVRLGTSESLPCTAEELSRSTTELLPRRPPSSSSSSSASSYTGRPIELDKMLLSKV KVPHTFLIHSYTRPTVCQACKKLLKGLFRQGLQCKDCKFNCHKRCATRVPNDCLGEALIN GDVPMEEATDFSEADKSALMDESEDSGVIPGSHSENALHASEEEEGEGGKAQSSLGYIPL MRVVQSVRHTTRKSSTTLREGWVVHYSNKDTLRKRHYWRLDCKCITLFQNNTTNRYYKEI PLSEILTVESAQNFSLVPPGTNPHCFEIVTANATYFVGEMPGGTPGGPSGQGAEAARGLX ETAIRQALMPVILQDAPSAPGHAPHRQASLSISVSNSQIQENVDIATVYQIFPDEVLGSG QFGVVYGGKHRKTGRDVAVKVIDKLRFPTKQESQLRNEVAILQSLRHPGIVNLECMFETP EKVFVVMEKLHGDMLEMILSSEKGRLPERLTKFLITQILVALRHLHFKNIVHCDLKPENV LLASADPFPQVKLCDFGFARIIGEKSFRRSVVGTPAYLAPEVLLNQGYNRSLDMWSVGVI  ${\tt MYVSLSGTFPFNEDEDINDQIQNAAFMYPASPWSHISAGAIDLINNLLQVKMRKRYSVDK}$ SLSHPWLQEYQTWLDLRELEGKMGERYITHESDDARWEQFAAEHPLPGSGLPTDRDLGGA CPPQDHDMQGLAERISVL

SEQ ID NO: 131\_AA127299\_H IQFIIVGAKDLLAMDSNGLSDPYIKITNLSQKTKVIKKTLTPTWNETFFVHFPEKTTLEL ECWDHDTFSDDFIGKASISLAEIPALAEVDMWIDMKTKKGEFAGK

2/113

#### FIGURE 1C

SEO ID NO: 132 AA316804 H  ${\tt MSANNSPPSAQKSVLPTAIPAVLPAASPCSSPKTGLSARLSNGSFSAPSLTNSRGSVHTV}$ SFLLQIGLTRESVTIEAQELSLSAVKDLVCSIVYQKFPECGFFGMYDKILLFRHDMNSEN ILQLITSADEIHEGDLVEVVLSALATVEDFQIRPHTLYVHSYKAPTFCDYCGEMLWGLVR QGLKCEGCGLNYHKRCAFKIPNNCSGVRKRRLSNVSLPGPGLSVPRPLQPEYVALPSEES HVHQEPSKRIPSWSGRPIWMEKMVMCRVKVPHTFAVHSYTRPTICQYCKRLLKGLFRQGM QCKDCKFNCHKRCASKVPRDCLGEVTFNGEPSSLGTDTDIPMDIDNNDINSDSSRGLDDT EEPSPPEDKMFFLDPSDLDVERDEEAVKTISPSTSNNIPLMRVVQSIKHTKRKSSTMVKE GWMVHYTSRDNLRKRHYWRLDSKCLTLFQNESGSKYYKEIPLSEILRISSPRDFTNISQG SNPHCFEIITDTMVYFVGENNGDSSHNPVLAATGVGLDVAQSWEKAIRQALMPVTPQASV CTSPGQGKDHKDLSTSISVSNCQIQENVDISTVYQIFADEVLGSGQFGIVYGGKHRKTGR DVAIKVIDKMRFPTKQESQLRNEVAILQNLHHPGIVNLECMFETPERVFVVMEKLHGDML EMILSSEKSRLPERITKFMVTQILVALRNLHFKNIVHCDLKPENVLLASAEPFPQVKLCD FGFARIIGEKSFRRSVVGTPAYLAPEVLRSKGYNRSLDMWSVGVIIYVSLSGTFPFNEDE DINDQIQNAAFMYPPNPWREISGEAIDLINNLLQVKMRKRYSVDKSLSHPWLQDYQTWLD LREFETRIGERYITHESDDARWEIHAYTHNLVYPKHFIMAPNPDDMEEDP

SEQ ID NO: 133 PKNBETA H MEEGAPRQPGPSQWPPEDEKEVIRRAIQKELKIKEGVENLRRVATDRRHLGHVQQLLRSS. NRRLEQLHGELRELHARILLPGPGPGPAEPVASGPRPWAEQLRARHLEALRRQLHVELKV KQGAENMTHTCASGTPKERKLLAAAQQMLRDSQLKVALLRMKISSLEASGSPEPGPELLA EELQHRLHVEAAVAEGAKNVVKLLSSRRTQDRKALAEAQAQLQESSQKLDLLRLALEQLL EQLPPAHPLRSRVTRELRAAVPGYPQPSGTPVKPTALTGTLQVRLLGCEQLLTAVPGRSP-AAALASSPSEGWLRTKAKHQRGRGELASEVLAVLKVDNRVVGQTGWGQVAEQSWDQTFVI PLERARELEIGVHWRDWRQLCGVAFLRLEDFLDNACHQLSLSLVPQGLLFAQVTFCDPVI ERRPRLQRQERIFSKRRGQDFLRRSQMNLGMAAWGRLVMNLLPPCSSPSTISPPKGCPRT PTTLREASDPATPSNFLPKKTPLGEEMTPPPKPPRLYLPQEPTSEETPRTKRPHMEPRTR RGPSPPASPTRKPPRLQDFRCLAVLGRGHFGKVLLVQFKGTGKYYAIKALKKQEVLSRDE IESLYCEKRILEAVGCTGHPFLLSLLVCFQTSSHARFVTEFVPGGDLMMQIHEDVFPEPQ ARFYVACVVLGLQFLHEKKIIYRDLKLDNLLLDAQGFLKIADFGLCKEGIGFGDRTSTFC GTPEFLAPEVLTQEAYTQAVDWWALGVLLYEMLVGECPFPGDTEEEVFDCIVNMDAPYPG FLSVQGLEFIQKLLQKCPEKRLGAGEQDAEEIKVQPFFRTTNWQALLARTIQPPFVPTLC - GPADLRYFEGEFTGLPPALTPPAPHSLLTARQQAAFRDFDFVSERFLEP

SEQ ID NO: 134\_AI021023\_M PKNBETA\_M
LKWDNLLLDAQGFLKIADFGLCKEGIGFGDRTSTFCGTPEFLAPEVLTQEAYTRAVDWWG
LGVLLYEMLVGECPFPGDTEEEVFDCIVNMDAPYPGFLSVQGLEFIQKLLQKCPEKRLGA
GEQDAEEIKVQPFFRTTNWQALLARTIQPPFVPTLCGPADLRYFEGEFTGLPPALTPPAP
HSLLTARQQAAFRDFDFVSERFLEP

SEQ ID NO: 135\_H19102\_H
GGNIRGPWARGWKSLWTGLGTIRSDLEELWELRGHHYLHQESLKPAPVLVEKPLPEWPVP
QFINLFLPEFPIRPIRGQQQLKILGLVAKGSFGTVLKVLDCTQKAVFAVKVVPKVKVLQR
DTVRQCKEEVSIQRQINHPFVHSLGDSWQGKRHLFIMCSYCSTDLYSLWSAVGCFPEASI
RLFAAELVLVLCYLHDLGIMHRDVKMENILLDERGHLKLTDFGLSRHVPQGAQAYTICGT
LQYMAPEVLSGGPYNHAADWWSLGVLLFSLATGKFPVAAERDHVAMLASVTHSDSEIPAS
LNQGLSLLLHELLCQNPLHRLRYLHHFQVHPFFRGVAFDPELLQKQPVNFVTETQATQPS
SAETMPFDDFDCDLESFLLYPIPA

PCT/US00/14842

#### FIGURE 1D

SEO ID NO: 136 AA476563 H

MEFFRIDSKDSASELLGLDFGEKLYSLKSEPLKPFFTLPDGDSASRSFNTSESKVEFKAQ
DTISRGSDDSVPVISFKDAAFDDVSGTDEGRPDLLVNLPGELESTREAAAMGPTKFTQTN
IGIIENKLLEAPDVLCLRLSTEQCQAHEEKGIEELSDPSGPKSYSITEKHYAQEDPRMLF
VAAVDHSSSGDMSLLPSSDPKFQGLGVVESAVTANNTEESLFRICSPLSGANEYIASTDT
LKTEEVLLFTDQTDDLAKEEPTSLFQRDSETKGESGLVLEGDKEIHQIFEDLDKKLALAS
RFYIPEGCIQRWAAEMVVALDALHREGIVCRDLNPNNILLNDRGHIQLTYFSRWSEVEDS
CDSDAIERMYCAPEVGAITEETEACDWWSLGAVLFELLTGKTLVECHPAGINTHTTLNMP
ECVSEEARSLIQQLLQFNPLERLGAGVAGVEDIKSHPFFTPVDWAELMR

SEQ ID NO: 137 AA626690 H

MLPFAPQDEPWDREMEVFSGGGASSGEVNGLKMVDEPMEEGEADSCHDEGVVKEIPITHH VKEGYEKADPAQFELLKVLGQGSFGKVFLVRKKTGPDAGQLYAMKVLKKASLKVRDRVRT KMERDILVEVNHPFIVKLHYAFQTEGKLYLILDFLRGGDVFTRLSKEVLFTEEDVKFYLA ELALALDHLHQLGIVYRDLKPENILLDEIGHIKLTDFGLSKESVDQEKKAYSFCGTVEYM APEVVNRRGHSQSADWWSYGVLMFEMLTGTLPFQGKDRNETMNMILKAKLGMPQFLSAEA QSLLRMLFKRNPANRLGSEGVEEIKRHLFFANIDWDKLYKREVQPPFKPASGKPDDTFCF DPEFTAKTPKDSPGLPASANAHQLFKGFSFVATSIAEEYKITPITSANVLPIVQINGNAA QFGEVYELKEDIGVGSYSVCKRCIHATTNMEFAVKIIDKSKRDPSEEIEILMRYGQHPNIITLKDVFDDGRYVYLVTDLMKGGELLDRILKQKCFSEREASDILYVISKTVDYLHCQGVVHRDLKPSNILYMDESASADSIRICDFGFAKQLRGENGLLLTPCYTANFVAPEVLMQQGYDAACDIWSLGVLFYTMLAGYTPFANGPNDTPEEILLRIGNGKFSLSGGNWDNISDGAKDLLSHMLHMDPHQRYTAEQILKHSWITHRDQLPNDQPKRNDVSHVVKGAMVATYSALTHKTFQPVLEPVAASSLAQRRSMKKRTSTGL

SEQ ID NO: 138 AA215680 H

MSLVACECLPSPGLEPEPCSRARSQAHVYLEQIRNRVALGVPDMTKRDYLVDAATQIRLA LERDVSEDYEAAFNHYQNGVDVLLRGIHVDPNKERREAVKLKITKYLRRAEEIFNCHLQR PLSSGASPSAGFSSLRLRPIRTLSSAVEQLRGCRVVGVIEKVQLVQDPATGGTFVVKSLP RCHMVSRERLTIIPHGVPYMTKLLRYFVSEDSIFLHLEHVQGGTLWSHLLSQAHSRHSGL SSGSTQERMKAQLNPHLNLLTPARLPSGHAPGQDRIALEPPRTSPNLLLAGEAPSTRPQR EAEGEPTARTSTSGSSDLPKAPGGHLHLQARRAGQNSDAGPPRGLTWVPEGAGPVLGGCG RGMDQSCLSADGAGRGCGRATWSVREEQVKQWAAEMLVALEALHEQGVLCRDLHPGNLLL DQAGHIRLTYFGQWSEVEPQCCGEAVDNLYSAPEVGGISELTEACDWWSFGSLLYELLTG MALSQSHPSGIQAHTQLQLPEWLSRPAASLLTELLQFEPTRRLGMGEGGVSKLKSHPFFS TIOWSKLVG

SEQ ID NO: 139 SGK H

MTVKTEAAKGTLTYSRMRGMVAILIAFMKQRRMGLNDFIQKIANNSYACKHPEVQSILKI SQPQEPELMNANPSPPPSPSQQINLGPSSNPHAKPSDFHFLKVIGKGSFGKVLLARHKAE EVFYAVKVLQKKAILKKKEEKHIMSERNVLLKNVKHPFLVGLHFSFQTADKLYFVLDYIN GGELFYHLQRERCFLEPRARFYAAEIASALGYLHSLNIVYRDLKPENILLDSQGHIVLTD FGLCKENIEHNSTTSTFCGTPEYLAPEVLHKQPYDRTVDWWCLGAVLYEMLYGLPPFYSR NTAEMYDNILNKPLQLKPNITNSARHLLEGLLQKDRTKRLGAKDDFMEIKSHVFFSLINW DDLINKKITPPFNPNVSGPNELRHFDPEFTEEPVPNSIGKSPDSVLVTASVKEAAEAFLG FSYAPPTDSFL

SEQ ID NO: 140 AA107515 M

MTVKAEAARSTLTYSRMRGMVAILIAFMKQRRMGLNDFIQKIASNTYACKHAEVQSILKM SHPQEPELMNANPSPPPSPSQQINLGPSSNPHAKPSDFHFLKVIGKGSFGKVLLARHKAE

4/113

#### FIGURE 1E

EVFYAVKVLQKKAILKKKEEKHIMSERNVLLKNVKHPFLVGLHFSFQTADKLYFVLDYIN GGELFYHLQRERCFLEPRARFYAAEIASALGYLHSLNIVYRDLKPENILLDSQGHIVLTD XFQLRRIEHNGTTSTFCGTPEYLAPEVLHKQPYDRTVDWWCLGAVLYEMLYGLPPFYSRN TAEMYDNILNKPLQLKPNITNSARHLLEGLLQKDRTKRLGAKDDFMEIKSHIFFSLINWD DLINKKITPPFNPNVSGPSDLRHFDPEFTEEPVPSSIGRSPDSILVTASVKEAAEAFLGF SYAPPVDSFL

SEQ ID NO: 141\_AA109508\_M
HLQRERRFLEPRARFYAAEVASAIGYLHSLNIIYRDLKPENILLDCQGHVVLTDFGLCKE
GVEPEDTTSTFCGTPEYLAPEVLRKEPYDRAVDWWCLGAVLYEMLHGLPPFYSQDVSQMY
ENILHQPLQIPGGRTVAACDLLQSLLHKDQRQRLGSKADFLEIKNHVFFSPINWDDLYHK
RLTPPFNPNVTGPADLKHFDPEFTQEAVSKSIGCTPDTVASSSGASSAFLGFSYAPEDDD
ILDC

SEQ ID NO: 142\_AA887783\_H
MQRDHTMDYKESCPSVXIPSSDEHREKKKRFTVYKVLVSVGRSEWFVFRRYAEFDKLYNT
LKKQFPAXALKIPAKRIFGDNFDPDFIKQRRAGLNEFIQNLVRYPELYNHPDVRAFLQMD
SPKHQSDPSEDEDERSSQKLHSTSQNINLGPSGNPHAKPTDFDFLKVIGKGSFGKVLLAK
RKLDGKFYAVKVLQKKIVLNRKEQKHIMAERNVLLKNVKHPFLVGLHYSFQTTEKLYFVL
DFVNGGEGHVVLTDFGLCKEGIAISDTTTTFCGTPEYLAPEVIRKQPYDNTVDWWCLGAV
LYEMLYGLPPFYCRDVAEMYDNILHKPLSLRPGVSLTAWSILEELLEKDRQNRLGAKEDF
LEIQNHPFFESLSWADLVQKKIPPPFNPNVAGPDDIRNFDTAFTEETVPYSVCVSSDYSI
VNASVLEADDAFVGFSYAPPSEDLFL

SEQ ID NO: 143\_R47805\_H
MAHQTGIHATEELKEFFAKARAGSVRLIKVVIEDEQLVLGASQEPVGRWDQDYDRAVLPL
LDAQQPCYLLYRLDSQNAQGFEWLFLAWSPDNSPVRLKMLYAATRATVKKEFGGGHIKDE
LFGTVKDDLSFAGYQKHLSSCAAPAPLTSAERELQQIRINEVKTEISVESKHQTLQGLAF
PLQPEAQRALQQLKQKMVNYIQMKLDLERETIELVHTEPTDVAQLPSRVPRDAARYHFFL
YKHTHEGDPLESVVFIYSMPGYKCSIKERMLYSSCKSRLLDSVEQDFHLEIAKKIEIGDG
AELTAEFLYDEVHPKQHAFKQAFAKPKGPGGKRGHKRLIRGPGENGDDS

SEQ ID NO: 144\_H60215\_H

MSKLRMKRRASDRGAGETSARAKALGSGISGNNAKRAGPFILGPRLGNSPVPSIVQCLAR

KDGTDDFYQLKILTLEERGDQGIESQEERQGKMLLHTEYSLLSLLHTQDGVVHHHGLFQD
RTCEIVEDTESSRMVKKMKKRICLVLDCLCAHDFSDKTADLINLQHYVIKEKRLSERETV

VIFYDVVRVVEALHQKNIVHRDLKLGNMVLNKRTHRITITNFCLGKHLVSEGDLLKDQRG

SPAYISPDVLSGRPYRGKPSDMWALGVVLFTMLYGQFPFYDSIPQELFRKIKAAEYTIPE

DGRVSENTVCLIRKLLVLDPQQRLAAADVLEALSAIIASWQSLSSLSGPLQVVPDIDDQM

SNADSSQEAKVTEECSQYEFENYMRQQLLLAEEKSSIHDTRSWVPKRQFGSAPPVRRLGH

DAQPMTSLDTAILAQRYLRK

SEQ ID NO: 145\_SGK324\_H

MASTRSIELEHFEERDKRPRPGSRRGAPSSSGGSSSSGPKGNGLIPSPAHSAHCSFYRTR

TLQALSSEKKAKKARFYRNGDRYFKGLVFAISSDRFRSFDALLIELTRSLSDNVNLPQGV

RTIYTIDGSRKVTSLDELLEGESYVCASNEPFRKVDYTKNINPNWSVNIKGGTSRALAAA

SSVKSEVKESKDFIKPKLVTVIRSGVKPRKAVRILLNKKTAHSFEQVLTDITEAIKXASG

VVKRLCTLDGKQVRVTCVHLPDFFGDDDVFIACGPEKFRYAQDDFVLDHSECRVLKSSYS

RSSAVKYSGSKSPGPSRRSQISAHGRSSSNVNGGPELDRCISPEGVNGNRCSESSTLLEK

YKIGKVIGDGNFAVVKECIDRSTGKEFALKIIDKAKCCGKEHLIENEVSILRRVKHPNII

#### FIGURE 1F

MLVEEMETATELFLVMELVKGGDLFDAITSSTKYTERDGSAMVYNLANALRYLHGLSIVH RDIKPENLLVCEYPDGTKSLKLGDFGLATVVEGPLYTVCGTPTYVAPXIIAETGYGLKVD IWAAGVITYILLCGFPPFRSENNLQEDLFDQILAGKLEFPAPYWDNITDSAKELISQMLQ VNVEARCTAGQILSHPWVSDDASQENNMQAEVTGKLKQHFNNALPKQNSTTTGVSVIMVS GRROVWPDCGAGLEVFELGSRELPSHGSWCLP

SEQ ID NO: 146\_W30246\_M SGK324\_M TKSSSSPTSPGSFRGLKISAQGRSSSNVNGGPELDRCLSPEGVNGNRCSESFPLLEKYR IGKVIGDGNFAVVKECVDRYTGKEFALKIIDKAKCCGKEHLIENEVSILRRVKHPNIIML VEEMETATDLFLVMELVKGGDLFDAITSSTKYTERDGSAMVYNLANALRYLHSLSIVHRD IKPENLLVCEYPDGTKSLKLGDFGLATVVEGPLYTVCGTPTYVAPEIIAETGYGLKVDVW AAGVITYILLCGFPPFRSENNLQEDLFDQILAGKLEFPAPYWDNITDSPCVCFRKCL

SEQ ID NO: 147\_AA383293\_H
PAAKRVVVYRNGDPFFPGSQLVVTQRRFPTMEAFLCEVTSAVQAPLAVRALYTPCHGHPV
TNLADLKNRGQYVAAGFERFHKLPPYQAFCLSVFRNGDLVSPPFSLKLSQAASQDWETVL
KLLTEKVKLQSGAVRLCTLEGLPLSAGKELVTGHYYVAVGEDEFKDLPYPALSTRGLLAA
GNEAHLRSGVGTVAGSPKPLGRKAKKETCLIVTLTLKYQQSETSRDGQSFPSGVIGVYGA
PHRRKETAGALEVADDEDTQTEEPLDQRAAQIVEQVTCLQDFFGDDDVFIACGPEKFRYA
QDDFVLDHSRRRLLREHQAGFEKLRRTRGEEKEAEKEKKPCMSGGRRMTLRDDQPAKLEK
EPKTRPEENKPERPSGRKPRPMGIIAANVEKHYETGRVIGDGNFAVVKECRHRETRQAYA
MKIIDKSRLKGKEDMVDSEILIIQSLSHPNIVKLHEVYETDMEIYLILEYVQGGDLFDAI
IESVKFPEPDAALMIMDLCKALVHMHDKSIVHRDLKPENLLVQRNEDKSTTLKLADFGLA
KHVVRPIFTVCGTPTYVAPEILSEKGYGLEVDMWAAGVILYILLCGFPPFRSPXXGDQDE
LFNIIQLGHFEFLPPYWDNISDAAKDLVSRLLVVDPKKRYTAHQVLQHPWIETAGKTNTV
KRQKQVSPSSDGHFRSQHKRVVEQVS

SEQ ID NO: 148\_AA197883\_M
MPTAPVLRPPPPPATPAPPAPSRPAPPIPGHRGPCDHSLKCLSSKISERKLPGPWLPAGR
GPLEKPVLGPRGAVMPLFSPQSSLHSVRAEHSPLKPRVVTVVKLGGQPLRKATLLLNRRS
VQTFEQLLSDISEALGFPRWKNDRVRKLFTLKGREVKSVSDFFREGDAFIAMGKEPLTLK
SIQLAMEELYPKNRALALAPHSRVPSPRLRSRLPSKLLKGSHRCGEAGSYSAEMESKAVS
RHQGKTSTVLAPEDKARAQKWVRGKQESEPGGPPSPGAATQEETHASGEKHLGVEIEKTS
GEIVRCEKCKRERELQLGLQREPCPLGTSELDLGRAQKRDSEKLVRTKSCRRPSKAKFTD
GEEGWKGDSHRGSPRDPPQEMRRPNSNSDKKEIRGSESQDSYPQGAPKAQKDFVEGPPAV
EEGPIDMRREDRHTCRSKHAAWLRREQQAEPPQLPRTRGEEKQAEHEKKPGGLGERRAPE
KESKRKLEEKRPERPSGRKPRPKGIISADVEKHYDIGGVIGDGNFATVKECRHRETKQAY
AMKMIDKSQLKGKEDIVDSEILIIQSLSHPNIVKLHEVYETEAEIYLIMEYVQGGDLFDA
IVENVKFPEPEAAVMITDLCKAFVHMHDKNIVHRDVKPENLLVQRNEDKSITLKLADFGL
AKYVVRPIFTVCGTPTYVAPEILSEKGYGLEVDMWAAGVILYILLCGFPPFRSPERDQDE
LFNIIQVGQFEFLSPYWDNISDAAKDLVRNLLEVDPKKRYTAEQVLQHPWIEMVGHTNTG
NSOKEESPNSLGHFQSQHKKVAEQMP

SEQ ID NO: 149\_DRAK2\_H
MSRRRFDCRSISGLTTTPQIPIKMENFNNFYILTSKELGRGKFAVVRQCISKSTGQEYA
AKFLKKRRRGQDCRAEILHEIAVLELAKSCPRVINLHEVYENTSEIILILEYAAGGEIFS
LCLPELAEMVSENDVIRLIKQILEGVYYLHQNNIVHLDLKPQNILLSSIYPLGDIKIVDF
GMSRKIGHACELREIMGTPEYLAPEILNYDPITTATDMWNIGIIAYMLLTHTSPFVGEDN
QETYLNISQVNVDYSEETFSSVSQLATDFIQSLLVKNPEKRPTAEICLSHSWLQQWDFEN

#### FIGURE 1G

LFHPEETSSSSQTQDHSVRSSEDKTSKSSCNGTCGDREDKENIPEDSSMVSKRFRFDDSL PNPHELVSDLLC

SEQ ID NO: 150\_W44160\_M DRAK2\_M
MSRRRFDCRSVSGLLTTTPQTPIKTENFNNFYTLTPKELGRGKFAVVRQCISKSTGQEYA
AKSLKKRRGQDCRAEILHEIAVLELARSCPHVINLHEVYENATEIILVLEYAAGGEIFN
LCLPELAEMVSENDVIRLIKQILEGVHYLHQNNIVHLDLKPQNILLSSIYPLGDIKIVDF
GMSRKIGNASELREIMGTPEYLAPEILNYDPITTATDMWNIGIIAYMLLTHTSPFVGEDN
QETYLNISQVNVDYSEEMFSSVSQLATDFIQSLLVKNPEKRPTAESCLSHSWLQQWDFGS
LFHPEETSGSSQIQDLTLRSSEEKTSKSSCNGSCGAREDKENIPEDGSLVSKRFRFDDSL
PSPHELVPDLFC

SEQ ID NO: 151\_H01248\_H, DRAK1\_H
MIPLEKPGSGGSSPGATSGSGRAGRGLSGPCRPPPPPQARGLLTEIRAVVRTEPFQDGYS
LCPGRELGRGKFAVVRKCIKKDSGKEFAAKFMRKRRKGQDCRMEIIHEIAVLELAQDNPW
VINLHEVYETASEMILVLEYAAGGEIFDQCVADREEAFKEKDVQRLMRQILEGVHFLHTR
DVVHLDLKPQNILLTSESPLGDIKIVDFGLSRILKNSEELREIMGTPEYVAPEILSYDPI
SMATDMWSIGVLTYVMLTGISPFLGNDKQETFLNISQMNLSYSEEFFDVLSESAVDFIRT
LLVKKPEDRATAEECLKHPWLTQSSIQEPSFRMEKALEEANALQEGHSVPEINSDTDKSE
TEESIVTEELIVVTSYTLGQCRQSEKEKMEQKAISKRFKFEEPLLQEIPGEFIY

SEQ ID NO: 152 AA021445 H MPARIGYYEIDRTIGKGNFAVVKRATHLVTKAKVAIKIIDKTQLDEENLKKIFREVQIMK MLCHPHIIRLYQVMETERMIYLVTEYASGGEIFDHLVAHGRMAEKEARRKFKQIVTAVYF CHCRNIVHRDLKAENLLLDANLNIKIADFGFSNLFTPGQLLKTWCGSPPYAAPELFEGKE YDGPKVDIWSLGVVLYVLVCGALPFDGSTLQNLRARVLSGKFRIPFFMSTECEHLIRHML VLDPNKRLSMEQICKHKWMKLGDADPNFDRLIAECQQLKEERQVDPLNEDVLLAMEDMGL DKEQTLQSLRSDAYDHYSAIYSLLCDRHKRHKTLRLGALPSMPRALAFQAPVNIQAEQAG TAMNISVPQVQLINPENQIVEPDGTLNLDSDEGEEPSPEALVRYLSMRRHTVGVADPRTE VMEDLQKLLPGFPGVNPQAPFLQVAPNVNFMHNLLPMQNLQPTGQLEYKEQSLLQPPTLQ LLNGMGPLGRRASDGGANIQLHAQQLLKRPRGPSPLVTMTPAVPAVTPVDEESSDGEPDQ EAVQRYLANRSKRHTLAMTNPTAEIPPDLQRQLGQQPFRSRVWPPHLVPDQHRSTYKDSN TLHLPTERFSPVRRFSDGAASIQAFKAHLEKMGNNSSIKQLQQECEQLQKMYGGQIDERT LEKTQQQHMLYQQEQHHQILQQQIQDSICPPQPSPPLQAACENQPALLTHQLQRLRIQPS SPPPNHPNNHLFRQPSNSPPPMSSAMIQPHGAASSSQFQGLPSRSAIFQQQPENCSSPPN VALTCLGMQQPAQSQQVTIQVQEPVDMLSNMPGTAAGSSGRGISISPSAGQMQMQHRTNL MATLSYGHRPLSKQLSADSAEAHSLNVNRFSPANYDQAHLHPHLFSDQSRGSPSSYSPST GVGFSPTQALKVPPLDQFPTFPPSAHQQPPHYTTSALQQALLSPTPPDYTRHQQVPHILQ GLLSPRHSLTGHSDIRLPPTEFAQLIKRQQQQRQQQQQQQQQQQQQEYQELFRHMNQGDAGSL APSLGGQSMTERQALSYQNADSYHHHTSPQHLLQIRAQECVSQASSPTPPHGYAHQPALM HSESMEEDCSCEGAKDGFQDSKSSSTLTKGCHDSPLLLSTGGPGDPESLLGTVSHAQELG IHPYGHQPTAAFSKNKVPSREPVIGNCMDRSSPGQAVELPDHNGLGYPARPSVHEHHRPR ALQRHHTIQNSDDAYVQLDNLPGMSLVAGKALSSARMSDAVLSQSSLMGSQQFQDGENEE CGASLGGHEHPDLSDGSQHLNSSCYPSTCITDILLSYKHPEVSFSMEQAGV

SEQ ID NO: 153\_2R22-5-11\_H MTAVYMNGGGLVNPHYARWDRRDSVESGCQTESSKEGEEGQPRQLTPFEKLTQDMSQDEK VVREITLGKRIGFYRIRGEIGSGNFSQVKLGIHSLTKEKVAIKILDKTKLDQKTQRLLSR EISSMEKLHHPNIIRLYEVVETLSKLHLVMEYAGGGELFGKISTEGKLSEPESKLIFSQI VSAVKHMHENQIIHRDLKAENVFYTSNTCVKVGDFGFSTVSKKGEMLNTFCGSPPYAAPE

PCT/US00/14842

#### FIGURE 1H

LFRDEHYIGIYVDIWALGVLLYFMVTGTMPFRAETVAKLKKSILEGTYSVPPHVSEPCHR LIRGVLQQIPTERYGIDCIMNDEWMQGVPYPTPLEPFQLDPKHLSETSTLKEEENEVKST LEHLGITEEHIRNNQGRDARSSITGVYRIILHRVQRKKALESVPVMMLPDPKERDLKKGS RVYRGIRHTSKFCSIL

SEQ ID NO: 154\_R31237\_1\_H, AAC33487

MSTRTPLPTVNERDTENHTSHGDGRQEVTSRTSRSGARCRNSIASCADEQPHIGNYRLLK
TIGKGNFAKVKLARHILTGREVAIKIIDKTQLNPTSLQKLFREVRIMKILNHPNIVKLFE
VIETEKTLYLIMEYASGGEVFDYLVAHGRMKEKEARSKFRQIVSAVQYCHQKRIVHRDLK
AENLLLDADMNIKIADFGFSNEFTVGGKLDTFCGSPPYAAPELFQGKKYDGPEVDVWSLG
VILYTLVSGSLPFDGQNLKELRERVLRGKYRIPFYMSTDCENLLKRFLVLNPIKRGTLEQ
IMKDRWINAGHEEDELKPFVEPELDISDQKRIDIMVGMGYSQEEIQESLSKMKYDEITAT
YLLLGRKSSELDASDSSSSSNLSLAKVRPSSDLNNSTGQSPHHKVQRSVSSSQKQRRYSD
HAGPAIPSVVAYPKRSQTSTADGDLKEDGISSRKSSGSAVGGKGIAPASPMLGNASNPNK
ADIPERKKSSTVPSSNTASGGMTRRNTYVCSERTTADRHSVIQNGKENSTIPDQRTPVAS
THSISSAATPDRIRFPRGTASRSTFHGQPRERRTATYNGPPASPSLSHEATPLSQTRSRG
STNLFSKLTSKLTRSRNVSAEQKDENKEAKPRSLRFTWSMKTTSSMDPGDMMREIRKVLD
ANNCDYEQRERFLLFCVHGDGHAENLVQWEMEVCKLPRLSLNGVRFKRISGTSIAFKNIA
SKIANELKL

SEQ ID NO: 155\_W90839\_M
KGPSWSSRSLGARCRNSIASCPEEQPHVGNYRLLRTIGKGNFAKVKLARHILTGREVAIK
IIDKTQLNPSSLQKLFREVRIMKGLNHPNIVKLFEVIETEKTLYLVMEYASAGEVFDYLV
SHGRMKEKEARAKFRQIVSAVHYCHQKNIVHRDLKAENLLLDAEANIKIADFGFSNEFTL
GSKLDTFCGSPPYAAPELFQGKKYDGPEVDIWSLGVILYTLVSGSLPFDGHNLKELRERV
LRGKYRVPFYMSTDCESILRRFLVLNPAKRCTLEQIMKDKWINIGYEGEELKPDTELKEE
RMPGRKASCSAVGSGSRGLPPSSPMVSSAHNPNKAEIPERRKDSTSTPNNLPPSMMTRRN
TYVCTERPGSERPSLLPNGKENSSGTSRVPPASPSSHSLAPPSGERSRLARGSTIRSTFH
GGQVRDRRAGSGSGGGVQNGPPASPTLAHEAAPLPSGRPRPTTNLFTKLTSKLTRRVTDE
PERIGGPEVTSCHLPWDKTETAPRLLRFPWSVKLTSSRPS

SEQ ID NO: 156 406786.5 H MEVGGLTVFEEDQRCLSQSLPLPVSAEGPAAQTTAEPSRSFSSAHRHLSRRNGLSRLCQS RTALSEDRWSSYCLSSLAAQNICTSKLHCPAAPEHTDPSEPRGSVSCCSLLRGLSSGWSS PLLPAPVCNPNKAIFTVDAKTTEILVANDKACGLLGYSSQDLIGQKLTQFFLRSDSDVVE ALSEEHMEADGHAAVVFGTVVDIITRSGEKIPVSVWMKRMRQERRLCCVVVLEPVERVST WVAFQSDGTITSCDSLFAHLHGYVSGEDVAGQHITDLIPSVQLPPSGQHIPKNLKIQRSV GRARDGTTFPLSLKLKSQPSSEEATTGEAAPVSGYRASVWVFCTISGLITLLPDGTIHGI NHSFALTLFGYGKTELLGKNITFLIPGFYSYMDLAYNSSLQLPDLASCLDVGNESGCGER TLDPWQGQDPAEGGQDPRINVVLAGGHVVPRDEIRKLMESQDIFTGTQTELIAGGQLLSC LSPOPAPGVDNVPEGSLPVHGEQALPKDQQITALGREEPVAIESPGQDLLGESRSEPVDV KPFASCEDSEAPVPAEDGGSDAGMCGLCQKAQLERMGVSGPSGSDLWAGAAVAKPQAKGQ LAGGSLLMHCPCYGSEWGLWWRSQDLAPSPSGMAGLSFGTPTLDEPWLGVENDREELQTC LIKEQLSQLSLAGALDVPHAELVPTECQAVTAPVSSCDLGGRDLCGGCTGSSSACYALAT DLPGGLEAVEAQEVDVNSFSWNLKELFFSDQTDQTSSNCSCATSELRETPSSLAVGSDPD VGSLQEQGSCVLDDRELLLLTGTCVDLGQGRRFRESCVGHDPTEPLEVCLVSSEHYAASD RESPGHVPSTLDAGPEDTCPSAEEPRLNVQVTSTPVIVMRGAAGLQREIQEGAYSGSCYH RDGLRLSIQFEVRRVELQGPTPLFCCWLVKDLLHSQRDSAARTRLFLASLPGSTHSTAAE LTGPSLVEVLRARPWFEEPPKAVELEGLAACEGEYSQKYSTMSPLGSGAFGFVWTAVDKG KNKEVVVKFIKKEKVLEDCWIEDPKLGKVTLEIAILSRVEHANIIKVLDIFENQGFFQLV

#### FIGURE 11

MEKHGSGLDLFAFIDRHPRLDEPLASYIFRQVRAGQSRLVSAVGYLRLKDIIHRDIKDEN IVIAEDFTIKLIDFGSAAYLERGKLFYTFCGTIEYCAPEVLMGNPYRGPELEMWSLGVTL YTLVFEENPFCELEETVEAAIHPPYLVSKELMSLVSGLLQPVPERRTTLEKLVTDPWVTQ PVNLADYTWEEVFRVNKPESGVLSAASLEMGNRSLSDVAQAQELCGGPVPGEAPNGQGCL HPGDPRLLTS

SEQ ID NO: 157\_AA544838\_M 406786\_M
TRPHPCLDEPLASFIFRQLVSAVGYLHSQGIIHRDIKDENIVIAEDFTIKLIDFGSAAYL
ERGKLFYTFCGTIEYCAPEVLIGNPYRGPELEMWSLGVTLYTLIFEENPFCEVEETMEAV
IHPPFLVSQELMSLLSGLLQPCPEQRTTLEKLIRDPWVTQPVNLASYTWEEVCRTNQPES
GLLSAASLEIGSRSPSEMAQREGLCGPPAPRETRGDQHCLHLKDPSLPVS

SEQ ID NO: 158\_AA785735 H  $\overline{\texttt{MVMADGPRHLQRGPVRVGFYDIEGTLGKGNFAVVKLGRHRITKTEVAIKIIDKSQLDAVN}$ LEKIYREVQIMKMLDHPHIIKLYQVMETKSMLYLVTEYAKNGEIFDYLANHGRLNESEAR RKFWQILSAVDYCHGRKIVHRDLKAENLLLDNNMNIKIADFGFGNFFKSGELLATWCGSP PYAAPEVFEGQQYEGPQLDIWSMGVVLYVLVCGALPFDGPTLPILRQRVLEGRFRIPYFM SEDCEHLIRRMLVLDPSKRLTIAQIKEHKWMLIEVPVQRPVLYPQEQENEPSIGEFNEQV LRLMHSLGIDQQKXIESLQNKSYNHFAAIYFLLVERLKSHRSSFPVEQRLDGRQRRPSTI AEQTVAKAQTVGLPVTMHSPNMRLLRSALLPQASNVEAFSFPASGCQAEAAFMEEECVDT PKVNGCLLDPVPPVLVRKGCQSLPSNMMETSIDEGLETEGEAEEDPAHAFEAFQSTRSGQ RRHTLSEVTNQLVVMPGAGKIFSMNDSPSLDSVDSEYDMGSVQRDLNFLEDNPSLKDIML  ${\tt ANQPSPRMTSPFISLRPTNPAMQALSSQKREVHNRSPVSFREGRRASDTSLTQGIVAFRQ}$ HLQNLARTKGILELNKVQLLYEQIGPEADPNLAPAAPQLQDLASSCPQEEVSQQQESVST LPASVHPQLSPRQSLETQYLQHRLQKPSLLSKAQNTCQLYCKEPPRSLEQQLQEHRLQQK RLFLQKQSQLQAYFNQMQIAESSYPQPSQQLPLPRQETPPPSQQAPPFSLTQPLSPVLEP SSEQMQYSPFLSQYQEMQLQPLPSTSGPRAAPPLPTQLQQQQPPPPPPPPPPPPRQPGAAPA PLQFSYQTCELPSAASPAPDYPTPCQYPVDGAQQSDLTGPDCPRSPGLQEAPSSYDPLAL SELPGLFDCEMLDAVDPQHNGYVLVN

SEQ ID NO: 159\_AA207220\_H
MESLVFARRSGPTPSAAELARPLAEGLIKSPKPLMKKQAVKRHHKHNLRHRYEFLETLG
KGTYGKVKKARESSGRLVAIKSIRKDKIKDEQDLMHIRREIEIMSSLNHPHIIAIHEVFE
NSSKIVIVMEYASRGDLYDYISERQQLSEREARHFFRQIVSAVHYCHQNRVVHRDLKLEN
ILLDANGNIKIADFGLSNLYHQGKFLQTFCGSPLYASPEIVNGKPYTGPEVDSWSLGVLL
YILVHGTMPFDGHDHKILVKQISNGAYREPPKPSDCLXGLIRWLLMVNPTRRATLEDVAS
HWWVNWGYATRVGEQEAPHEGGHPGSDSARASMADWLRRSSRPLLENGAKVCSFFKQHAP
GGGSTTPGLERQHSLKKSRKENDMAQSLHSDTADDTAHRPGKSNLKLPKGILKKKVSASA
EGVQEDPPELSPIPASPGQAAPLLPKKGILKKPRQRESGYYSSPEPSESGELLDAGDVFV
SGDPKEQKPPQASGLLLHRKGILKLNGKFSQTALELAAPTTFGSLDELAPPRPLARASRP
SGAVSEDSILSSESFDQLDLPERLPEPPLRGCVSVDNLTGLEEPPSEGPGSCLRRWRQDP
LGDSCFSLTDCQEVTATYRQALRVCSKLT

SEQ ID NO: 160\_AA426580\_H, MAK\_V\_H
MPAAAGDGLLGEPAAPGGGGGAEDAARPAAACEGSFLPAWVSGVPRERLRDFQHHKRVGN
YLIGSRKLGEGSFAKVREGLHVLTGEKVAIKVIDKKRAKKDTYVTKNLRREGQIQQMIRH
PNITQLLDILETENSYYLVMELCPGGNLMHKIYEKKRLEESEARRYIRQLISAVEHLHRA
GVVHRDLKIENLLLDEDNNIKLIDFGLSNCAGILGYSDPFSTQCGSPAYAAPELLARKKY
GPKIDVWSIGVNMYAMLTGTLPFTVEPFSLRALYQKMVDKEMNPLPTQLSTGAISFLRSL
LEPDPVKRPNIQQALANRWLNENYTGKVPCNVTYPNRISLEDLSPSVVLHMTEKLGYKNS

#### FIGURE 1J

DVINTVLSNRACHILAIYFLLNKKLERYLSGKSDIQDSLCYKTRLYQIEKYRAPKESYEA SLDTWTRDLEFHAVQDKKPKEQEKRGDFLHRPFSKKLDKNLPSHKQPSGSLMTQIQNTKA LLKDRKASKSSFPDKDSFGCRNIFRKTSDSNCVASSSMEFIPVPPPRTPRIVKKPEPHQP GPGSTGIPHKEDPLMLDMVRSFESVDRDDHVEVLSPSHHYRILNSPVSLARRNSSERTLS PGLPSGSMSPLHTPLHPTLVSFAHEDKNSPPKEEGLCCPPPVPSNGPMQPLGSPNCVKSR GRFPMMGIGQMLRKRHQSLQPSADRPLEASLPPLQPLAPVNLAFDMADGVKTQC

SEO ID NO: 161 Z36720 H MDTKLNMLNEKVDQLLHFQEDVTEKLQSMCRDMGHLERGLHRLEASRAPGPGGADGVPHI DTQAGWPEVLELVRAMQQDAAQHGARLEALFRMVAAVDRAIALVGATFQKSKVADFLMQG RVPWRRGSPGDSPEEWVKEEEVCFMPPVPPAPGAAGQSLQKDKGELSAEQGIWATLMTLV  ${\tt IMVTAANKERVEEEGGKPKHVLSTSGVQSDAREPGEESQKADVLEGTAERLPPIRASGLG}$ ADPAQAVVSPGQGDGVPGPAQAFPGHLPLPTKVEAKAPETPSENLRTGLELAPAPGRVNV VSPSLEVAPGAGQGASSSRPDPEPLEEGTRLTPGPGPQCPGPPGLPAQARATHSGGETPP RAALLKGAVAPGFSRRDLVFPSIFCACLGISIHIQEMDTPGEMLMTGRGSLGPTLTTEAP AAAQPGKQGPPGTGRCLQAPGTEPGEQTPEGARELSPLQESSSPGGVKAEEEQRAGAEPG TRPSLARSDDNDHEVGALGLQQGKSPGAGNPEPEQDCAARAPVRAEAVRRMPPGAEAGSV VLDDSPAPPAPFEHRVVSVKETSISAGYEVCQHEVLGGGRFGQVHRCTEKSTGLPLAAKI IKVKSAKDREDVKNEINIMNQLSHVNLIQLYDAFESKHSCTLVMEYVDGGELFDRITDEK YHLTELDVVLFTRQICEGVHYLHQHYILHLDLKPENILCVNQTGHQIKIIDFGLARRYKP REKLKVNFGTPEFLAPEVVNYEFVSFPTDMWSVGVITYMLLSGLSPFLGETDAETMNFIV NCSWDFDADTFEGLSEEAKDFVSRLLVKEKSCRMSATQCLKHEWLNNLPAKASRSKTRLK SQLLLQKYIAQRKWKKHFYVVTAANRLRKFPTSP

SEO ID NO: 162 SGK088 H GEMALFECLVAGPTDVEVDWLCRGRLLQPALLKCKMHFDGRKCKLLLTSVHEDDSGVYTC KLSTAKDELTCSARLTVRPSLAPLFTRLLEDVEVLEGRAARFDCKISGTPPPVVTWTHFG CPMEESENLRLRQDGGLHSLHIAHVGSEDEGLYAVSAVNTHGQAHCSAQLYVEEPRTAAS GPSSKLEKMPSIPEEPEQGELERLSIPDFLRPLQDLEVGLAKEAMLECQVTGLPYPTISW FHNGHRIQSSDDRRMTQYRDVHRLVFPAVGPQHAGVYKSVIANKLGKAACYAHLYVTDVV PGPPDGAPQVVAVTGRMVTLTWNPPRSLDMAIDPDSLTYTVQHQVLGSDQWTALVTGLRE PGWAATGLRKGVQHIFRVLSTTVKSSSKPSPPSEPVQLLEHGPTLEEAPAMLDKPDIVYV VEGQPASVTVTFNHVEAQVVWRSCRGALLEARAGVYELSQPDDDQYCLRICRVSRRDMGA LTCTARNRHGTQTCSVTLELAEAPRFESIMEDVEVGAGETARFAVVVEGKPLPDIMWYKD EVLLTESSHVSFVYEENECSLVVLSTGAQDGGVYTCTAQNLAGEVSCKAELAVHSAQTAM EVEGVGEDEDHRGRRLSDFYDIHQEIGRGAFSYLRRIVERSSGLEFAAKFIPSQAKPKAS ARREARLLARLQHDCVLYFHEAFERRRGLVIVTELCTEELLERIARKPTVCESEIRAYMR QVLEGIHYLHQSHVLHLDVKPENLLVWDGAAGEQQVRICDFGNAQELTPGEPQYCQYGTP EFVAPEIVNQSPVSGVTDIWPVGVVAFLCLTGISPFVGENDRTTLMNIRNYNVAFEETTF LSLSREARGFLIKVLVQDRLRPTAEETLEHPWFKTQAKGAEVSTDHLKLFLSRRRWQRSQ ISYKCHLVLRPIPELLRAPPERVWVTMPRRPPPSGGLSSSSDSEEEELEELPSVPRPLQP EFSGSRVSLTDIPTEDEALGTPETGAATPMDWQEQGRAPSQDQEAPSPEALPSPGQEPAA GASPRRGELRRGSSAESALPRAGPRELGRGLHKAASVELPQRRSPGPGATRLARGGLGEG EYAQRLQALRQRLLRGGPEDGKVSGLRGPLLESLGGRARDPRMARAASSEAAPHHQPPLE NRGLQKSSSFSQGEAEPRGRHRRAGAPLEIPVARLGARRLQESPSLSALSEAQPSSPARP SAPKPSTPKSAEPSATTPSDAPQPPAPQPAQDKAPEPRPEPVRASKPAPPPQALQTLALP LTPYAQIIQSLQLSGHAQGPSQGPAAPPSEPKPHAAVFARVASPPPGAPEKRVPSAGGPP VLAEKARVPTVPPRPGSSLSSSIENLESEAVFEAKFKRSRESPLSLGLRLLSRSRSEERG PFRGAEEEDGIYRPSPAGTPLELVRRPERSRSVQDLRAVGEPGLVRRLSLSLSQRLRRTP PAQRHPAWEARGGDGESSEGGSSARGSPVLAMRRRLSFTLERLSSRLQRSGSSEDSGGAS

#### FIGURE 1K

GRSTPLFGRLRRATSEGESLRRLGLPHNQLAAQAGATTPSAESLGSEASATSGSSAPGES
RSRLRWGFSRPRKDKGLSPPNLSASVQEELGHQYVRSESDFPPVFHIKLKDQVLLEGEAA
TLLCLPAACPAPHISWMKDKKSLRSEPSVIIVSCKDGRQLLSIPRAGKRHAGLYECSATN
VLGSITSSCTVAVARVPGKLAPPEVTQTYQDTALVLWKPGDSRAPCTYTLERRVDGESVW
HPVSSGIPDCYYNVTHLPVGVTVRFRVACANRAGQGPFSNSSEKVFVRGTQDSSAVPSAA
HQEAPVTSRPARARPPDSPTSLAPPLAPAAPTPPSVTVSPSSPPTPPSQALSSLKAVGPP
PQTPPRRHRGLQAARPAEPTLPSTHVTPSEPKPFVLDTGTPIPASTPQGVKPVSSSTPVY
VVTSFVSAPPAPEPPAPEPPPEPTKVTVQSLSPAKEVVSSPGSSPRSSPRPEGTTLRQGP
PQKPYTFLEEKARGRFGVVRACRENATGRTFVAKIVPYAAEGKPRVLQEYEVLRTLHHER
IMSLHEAYITPRYLVLIAESCGNRELLCGLSDRFRYSEDDVATYMVQLLQGLDYLHGHHV
LHLDIKPDNLLLAPDNALKIVDFGSAQPYNPQALRPLGHRTGTLEFMAPEMVKGEPIGSA
TDIWGAGVLTYIMLSGRSPFYEPDPQETEARIVGGRFDAFQLYPNTSQSATLFLRKVLSV
HPWSRPSLQDCLAHPWLQDAYLMKLRRQTLTFTTNRLKEFLGEQRRRRAEAATRHKVLLR
SYPGGP

SEQ ID NO: 163\_AA542015\_M SGK088\_M
ATDIWGAGVLTYIMLSGYSPFYEPDPQETEARIVGGRFDAFQLYPNTSQSATLFLRKVLS
VHPWSRPSLQDCLAHPWLQDAYLMKLRRQTLTFTTNRLKEFLGEQRRRRAEAATRHKVLL
RSYPGSP

SEQ ID NO: 164 R19772\_H MKGGDRAYTRGPSLGWLFAKCCCCFPCRDAYSHSSSENGGKSESVANLQAQPSLNFIHSS PGPKRSTNTLKKWLTSPVRRLNSGKADGNIKKQKKVRDGRKSFDLGSPKPGDETTPQGDS ADESKKGWGEDEPDEESHTPLPPPMKIFDNDPTQDEMSSSLLAARQASTEVPTAADLVNA IEKLVKNKLSLEGSSYRGSLKDPAGCLNEGMAPPTPPKNPEEEQKAKALRGRMFVLNELV QTEKDYVKDLGIVVEGFMKRIEEKGVPEDMRGKDKIVFGNIHQIYDWHKDFFLAELEKCI QEQDRLAQLFIKHERKLHIYVWYCQNKPRSEYIVAEYDAYFEEVKQEINQRLTLSDFLIK PIQRITKYQLLLKDFLRYSEKAGLECSDIEKAVELMCLVPKRCNDMMNLGRLQGFEGTLT AQGKLLQQDTFYVIELDAGMQSRTKERRVFLFEQIVIFSELLRKGSLTPGYMFKRSIKMN YLVLEENVDNDPCKFALMNRETSERVVLQAANADIQQAWVQDINQVLETQRDFLNALQSP IEYQRKERSTAVMRSQPARLPQASPRPYSSVPAGSEKPPKGSSYNPPLPPLKISTSNGSP GFEYHQPGDKFEASKNDLGGCNGTSSMAVIKDYYALKENEICVSQGEVVQVLAVNQQNMC LVYQPASDHSPAAEGWVPGSILAPLTKATAAESSDGSIKKSCSWHTLRMRKRAEVENTGK NEATGPRKPKDILGNKVSVKETNSSEESECDDLDPNTSMEILNPNFIQEVAPEFLVPLVD VTCLLGDTVILQCKVCGRPKPTITWKGPDQNILDTDNSSATYTVSSCDSGEITLKICNLM PQDSGIYTCIATNDHGTTSTSATVKVQGVPAAPNRPIAQERSCTSVILRWLPPSSTGNCT ISGYTVEYREEGSQIWQQSVASTLDTYLVIEDLSPGCPYQFRVSASNPWGISLPSEPSEF VRLPEYDAAADGATISWKENFDSAYTELNEIGRGRFSIVKKCIHKATRKDVAVKFVNKKM KKKEQAAHEAALLQHLQHPQYITLHDTYESPTSYILILELMDDGRLLDYLMNHDELMEEK VAFYIRDIMEALQYLHNCRVAHLDIKPENLLIDLRIPVPRVKLIDLEDAVQISGHFHIHH LLGNPEFAAPEVIQGIPVSLGTDIWSIGVLTYVMLSGVSPFLDESKEETCINVCRVDFSF PHEYFCGVSNAARDFINVILQEDFRRRPTAATCLQHPWLQPHNGSYSKIPLDTSRLACFI ERRKHONDVRPIPNVKSYIVNRVNOGT

SEQ ID NO: 165\_5R72\_8\_2\_H
MADSGLDKKSTKCPDCSSASQKDVLCVCSSKTRVPPVLVVEMSQTSSIGSAESLISLERK
KEKNINRDITSRKDLPSRTSNVERKASQQQWGRGNFTEGKVPHIRIENGAAIEEIYTFGR
ILGKGSFGIVIEATDKETETKWAIKKVNKEKAGSSAVKLLEREVNILKSVKHEHIIHLEQ
VFETPKKMYLVMELCEDGELKEILDRKGHFSENETRWIIQSLASAIAYLHNNDIVHRDLK
LENIMVKSSLIDDNNEINLNIKVTDFGLAVKKQSRSEAMLQATCGTPIYMAPEVISAHDY

#### FIGURE 1L

SQQCDIWSIGVVMYMLLRGEPPFLASSEAKLFELIRKGELHFENAVWNSISDCAKSVLKQ LMKVDPAHRITAKELLDNQWLTGNKLSSVRPTNVLEMMKEWKNNPESVEENTTEEKNKPS TEEKLKSYQPWGNVPETNYTSDEEEEKQSTAYEKQFPATSKDNFDMCSSSFTSSKLLPAE IKGEMEKTPVTPSQGTATKYPAKSGALSRTKKKL

SEQ ID NO: 166\_SGK309\_H

MQCLAAALKDETNMSGGGEQADILPANYVVKDRWKVLKKIGGGGFGEIYEAMDLLTRENV

ALKVESAQQPKQVLKMEVAVLKKLQGSGLGQGDGKEEMMKPGAKRGKDHVCRFIGCGRNE

KFNYVVMQLQGRNLADLRRSQPRGTFTLSTTLRLGKQILESIEAIHSVGFLHRDIKPSNF

AMGRLPSTYRKCYMLDFGLARQYTNTTGDVRPPRNVAGFRGTVRYASVNAHKNREMGRHD

DLWSLFYMLVEFAVGQLPWRKIKDKEQVGMIKEKYEHRMLLKHMPSEFHLFLDHIASLDY

FTKPDYQLIMSVFENSMKERGIAENEAFDWEKAGTDALLSTSTSTPPPAEHPADGSHVWG

GQCDASAWGPAPGEHRGCATGRAPEXPGECTPNSAREALXGAGPQSPPCPPPRGSXGXSL

GGDRCQPEQTPDQHRQSNCRQGEGRGWPFLSPPIPSLVPLPCSSXAPCPPPISLLARPLF

PVPSPALASLCLPSSSSSSVSFTLRRPSA

SEQ ID NO: 167\_AA234451\_H
MSGGGEQLDILSVGILVKERWKVLRKIGGGGFGEIYDALDMLTRENVALKVESAQQPKQV
LKMEVAVLKKLQGKDHVCRFIGCGRNDRFNYVVMQLQGRNLADLRRSQSRGTFTISTTLR
LGRQILESIESIHSVGSXHRDIKPSNFAMGRFPSTCRKCYMLDFGLARQFTNSCGDVRPP
RAVAGFRGTVRYASINAHRNREMGRHDDLWSLFYMLVEFVVGQLPWRKIKDKEQVGSIKE
RYDHRLMLKHLPPEFSIFLDHISSLDYFTKPDYQLLTSVFDNSIKTFGVIESDPFDWEKT
GNDGSLTTTTTSTTPQLHTRLTPAAIGIANATPIPGDLLRENTDEVFPDEQLSDGENGIP
VGVSPDKLPGSLGHPRPQEKDVWEEMDANKNKIKLGICKAATEEENSHGQANGLLNAPSL
GSPIRVRSEITQPDRDIPLVRKLRSIHSFELEKRLTLEPKPDTDKFLETWYKIVYFSF

SEQ ID NO: 168\_AA435956\_H
TFTIFFEMTVFDLEAKSARGGSNLLMDSVSSFQLFMFQLLRGLAYIHHQHVLHRDLKPQN
LLISHLGELKLADFGLARAKSIPSQTYSSEVVTLWYRPPDALLGATEYSSELDIWGAGCI
FIEMFQGQPLFPGVSNILEQLEKIWEVLGVPTEDTWPGVSKLPNYNPEWFPLPTPRSLHV
VWNRLGRVPEAEDLASQMLKGFPRDRVSAQEALVHDYFSALPSQLYQLPDEESLFTVSGV
RLKPEMCDLLASYQKGHHPAQFSKCW

SEQ ID NO: 169\_AA626859\_H
NGVADGVIKSVLWQTLQALNFCHIHNCIHRDIKPENILITKQGIIKICDFGFAQILIPGD
AYTDYVATRWYRAPELLVGDTQYGSSVDIWAIGCVFAELLTGQPLWPGKSDVDQLYLIIR
TLGKLIPRHQSIFKSNGFFHGISIPEPEDMETLEEKFSDVHPVALNFMKGCLKMNPDDRL
TCSQLLESSYFDSFQEAQIKRKARNEGRNRRRQQNQLLPLIPGSHISPTPDGRKQVLQLK
FDHLPNI

SEQ ID NO: 170\_AA061797\_M
KIALREIRMLKLKHPNLVNLIEVFRRKRKMHLVFEYCDHTLLNELERNPNGVSDGVIKSV
LWQTLQALNFCHKHNCIHRDVKPENILITKQGMIKICDFGFARILIPGDAYTDYVATRWY
RAPELLVGDTKYGSSVDVWAVGCVFAELLTGQPLWPGKSDVDQLYLIIRTLGKLIPRHQS
IFRSNQFFRGISIPEPEDMETLEEKFSNVQPVALSFMKGCLKMNPDERLTCAQLLDSAYF
ESFQEDQMKRKARSEGRSRRRQQNQLLPLIPGSHISPTPDGRKQVVQLKFDHLPNI

SEQ ID NO: 171\_AA397553\_H MPNSERHGGKKDGSGGASGTLQPSSGGGSSNSRERHRLVSKHKRHKSKHSKDMGLVTPEA ASLGTVIKPLVEYDDISSDSDTFSDDMAFKLDRRENDERRGSDRSDRLHKHRHHQHRRSR

#### FIGURE 1M

DLLKAKQTEKEKSQEVSSKSGSMKDRISGSSKRSNEETDDYGKAQVAKSSSKESRSSKLH KEKTRKERELKSGHKDRSKSHRKRETPKSYKTVDSPKRRSRSPHRKWSDSSKQDDSPSGA SYGQDYDLSPSRSHTSSNYDSYKKSPGSTSRRQSVSPPYKEPSAYQSSTRSPSPYSRRQR SVSPYSRRRSSSYERSGSYSGRSPSPYGRRRSSSPFLSKRSLSRSPLPSRKSMKSRSRSP AYSRHSSSHSKKKRSSSRSRHSSISPVRLPLNSSLGAELSRKKKERAAAAAAAKMDGKES KGSPVFLPRKENSSVEAKDSGLESKKLPRSVKLEKSAPDTELVNVTHLNTEVKNSSDTGK VKLDENSEKHLVKDLKAQGTRDSKPIALKEEIVTPKETETSEKETPPPLPTIASPPPPLP TTTPPPQTPPLPPIPALPQQPPLPPSQPAFSQVPASSTSTLPPSTHSKTSAVSSQAN SQPPVQVSVKTQVSVTAAIPHLKTSTLPPLPLPPLLPGGDDMDSPKETLPSKPVKKEKEQ RTRHLLTDLPLPPELPGGDLSPPDSPEPKAITPPQQPYKKRPKICCPRYGERRQTESDWG KRCVDKFDIIGIIGEGTYGQVYKARDKDTGELVALKKVRLDNEKEGFPITAIREIKILRQ LIHRSVVNMKEIVTDKQDALDFKKDKGAFYLVFEYMDHDLMGLLESGLVHFSEDHIKSFM KQLMEGLEYCHKKNFLHRDIKCSNILLNNSGQIKLADFGLARLYNSEESRPYTNKVITLW YRPPELLLGEERYTPAIDVWSCGCILGELFTKKPIFQANLELAQLELISRLCGSPCPAVW PDVIKLPYFNTMKPKKQYRRRLREEFSFIPSAALDLLDHMLTLDPSKRCTAEQTLQSDFL KDVELSKMAPPDLPHWQDCHELWSKKRRRQRQSGVVVEEPPPSKTSRKETTSGTSTEPVK NSSPAPPQPAPGKVESGAGDAIGLADITQQLNQSELAVLLNLLQSQTDLSIPQMAQLLNI HSNPEMQQQLEALNQSISALTEATSQQQDSETMAPEESLKEAPSAPVILPSAEQMTLEAS STPADMQNILAVLLSQLMKTQEPAGSLEENNSDKNSGPQGPRRTPTMPQEEAAACPPHIL PPEKRPPEPPGPPPPPPPPPLVEGDLSSAPQELNPAVTAALLQLLSQPEAEPPGHLPHEH QALRPMEYSTRPRPNRTYGNTDGPETGFSAIDTDERNSGPALTESLVQTLVKNRTFSGSL SHLGESSSYQGTGSVQFPGDQDLRFARVPLALHPVVGQPFLKAEGSSNSVVHAETKLQNY GELGPGTTGASSSGAGLHWGGPTQSSAYGKLYRGPTRVPPRGGRGRGVPY

SEQ ID NO: 172\_AA789239\_H
MEMYETLGKVGEGSYGTVMKCKHKNTGQIVAIKIFYERPEQSVNKIAMREIKFLKQFHHE
NLVNLIEVFRQKKKIHLVFEFIDHTVLDELQHYCHGLESKRLRKYLFQILRAIDYLHSNN
VIIHRDIKPENILVSQSGITKLCDFGFARTLAAPGDIYTDYVATRWYRAPELVLKDTSYG
KYVPVDIWALGCMIIEMATGNPYLPSSSDLDLLHKIVLKVXFMPELKAKLLQEAKVNSLI
KPKESSKENELRKDERKTVYTNTLLSSSVLGKEIEKEKKPKEIKVRVIKVKGGRGDISEP
KKKEYEGGLGQQDANENVHPMSPDTKLVTIEPPNPINPSTNCNGLKENPHCGGSVTMPPI
NLTNSNLMAANLSSNLFHPSVRLTERAKKRRTSSQSIGQVMPNSRQEDPGPIQSQMEKGI
FNERTGHSDQMANENKRKLNFSRSDRKEFHFPELPVTIQSKDTKGMEVKQIKMLKRESKK
TESSKIPTLLNVDQNQEKQEFIPLSLLSACCPIFTNICSQLTIRVEMAIARGRI

SEQ ID NO: 173\_AA124976\_M
LADIVHACLQIDPAERTSSTDLLRHDYFTRDGFIEKFIPELRAKLLQEAKVNSFIKPKEN
FKENEPVRDEKKSVFTNTLLYGNPSLYGKEVDRDKRAKELKVRVIKAKGGKGDVPDQKKP
EYEGDHRQQGTADDTQPSSLDKKPSVLELTNPLNPSENSDGVKEDPHAGGCMIMPPINLT
SSNLLAANLSSNLSHPNSRLTERTKKRRTSSQTIGQTLSNSRQEDTGPTQVQTEKGAFNE
RTGQNDQISSGNKRKLNFPKCDRKEFHFPELPFTVQAKEMKGMEVKQIKVLKRESKKTDS
SKIPTLLSMDPNQEKQEGGDGDCEGKNLKRNRFFFSR

SEQ ID NO: 174\_AA575635\_M CCRK\_M SASGQLKIADFGLARVFSPDGGRLYTHQVATRWYRAPELLYGARQYDQGVDLWAVGCIMG ELLNGSPLFPGENDIEQLCCVLRILGTPSPRVWPEITELPDYNKISFEEQAPVPLEEVLP DASPQALDLLGQFLLYPPRQRIAASQALLHQYFFTAPLPAHPSELPIPQRPGGPAPKAHP GPPHVHDFHVDRPIEESLLNPELIRPFIPEG

#### FIGURE 1N

SEQ ID NO: 175\_AA631990\_H
MITSISTEKSGHTHYPFMITTLQYYRGRGGKTAVWRHFSAEGPFAFAEMRHSKRTHCPDW
DSRESWGHESYRGSHKRKRRSHSSTQENRHCKPHHQFKESDCHYLEARSLNERDYRDRRY
VDEYRNDYCEGYVPRHYHRDIESGYRIHCSKSSVRSRRSSPKRKRNRHCSSHQSRSXEIV
DTLGEGAFGKVVECIDHGMDGMHVAVKIVKNVGRYREAARSEIQVLEHLNSTDPNSVFRC
VQMLEWFDHHGHVCIVFELLGLSTYDFIKENSFLPFQIDHIRQMAYQICQSINFLHHNKL
THTDLKPENILFVKSDYVVKYNSKMKRDERTLKNTDIKVVDFGSATYDDEHHSTLVSTRH
YRAPEVILALGWSQPCDVWSIGCILIEYYLGFTVFQTHDSKEHLAMMERILGPIPQHMIQ
KTRKRKYFHHNQLDWDEHSSAGRYVRRRCKPLKEFMLCHDEEHEKLFDLVRRMLEYDPTQ
RITLDEALOHPFFDLLKKK

SEQ ID NO: 176\_AA557536\_H
MCTVVDPRIVRRYLLRRQLGQGRTFREITLLQVSGLGPPVQSPCPGTDLSRQERNWPSWA
PEHSPSWPSSRLRLSPQEFGDHPNIISLLDVIRAENDRDIYLVFEFMDTDLNAVIRKGGL
LQDVHVRSIFYQLLRATRFLHSGHVVHRDQKPSNVLLDANCTVKLCDFGLARSLGDLPEG
PEDQAVTEYVATRWYRAPEVLLSSHRYTASCPRYTLGVDMWSLGCILGEMLRGRPLFPGT
STLHQLELILETIPPPSEEXRPRQTLDALLPPDTSPEALDLLRRLLVFAPDKRLSATQAL
QHPYVQRFHCPSDEWAREADVRPRAHEGVQLSVPEYRSRVYQMILECGGSSGTSREKGPE
GVSPSQAHLHKPRADPQLPSRTPVQGPRPRPQSSPGHDPAEHESPRAAKNVPRQNSAPLL
QTALLGNGERPPGAKEAPPLTLSLVKPSGRGAAPSLTSQAAAQVANQALIRGDWNRGGGV
RVASVQQVPPRLPPEARPGRRMFSTSALQGAQGGARALLGGYSQAYGTVCHSALGHLPLL
EGHHV

SEQ ID NO: 177\_N28606\_H, MOK\_H
MKNYKAIGKIGEGTFSEVMKMQSLRDGNYYACKQMKQRFESIEQVNNLREIQALRRLNPH
PNILMLHEVVFDRKSGSLALICELMDMNIYELIRGRRYPLSEKKIMHYMYQLCKSLDHIH
RNGIFHRDVKPENILIKQDVLKLGDFGSCRSVYSKQPYTEYISTRWYRAPECLLTDGFYT
YKMDLWSAGCVFYEIASLQPLFPGVNELDQISKIHDVIGTPAQKILTKFKQSRAMNFDFP
FKKGSGIPLLTTNLSPQCLSLLHAMVAYDPDERIAAHQALQHPYFQEQRKTEKRALGSHR
KAGFPEHPVAPEPLSNSCQISKEGRKQKQSLKQEEDRPKRRGPAYVMELPKLKLSGVVRL
SSYSSPTLQSVLGSGTNGRVPVLRPLKCIPASKKTDPQKDLKPAPQQCRLPTIVRKGGR

SEQ ID NO: 178\_AB023153\_H, ICK\_H
MNRYTTIRQLGDGTYGSVLLGRSIESGELIAIKKMKRKFYSWEECMNQREVKSLKKLNHA
NVVKLKEVIRENDHLYFIFEYMKENLYQLIKERNKLFPESAIRNIMYQILQGLAFIHKLG
FFHRDLKPENLLCMGPELVKIADFGLAREIRSKPPYTDYVSTRWYRAPEVLLRSTNYSSP
IDVWAVGCIMAEVYTLRPLFPGASEIDTIFKICQVLGTPKKTDWPEGYQLSSAMNFRWPQ
CVPNNLKTLIPNASSEAVQLLRDMLQWDPKKRPTASQALRYPYFQVGHPLGSTTQNLQDS
EKPQKGILERAGPPPYIKPVPPAQPPAKPHTRISSRQHQASQPPLHLTYPYKAEVSRTDH
PSHLQEDKPSPLLFPSLHNKHPQSKITAGLEHKNGEIKPKSRRRWGLISRSTKDSDDWAD
LDDLDFSPSLSRIDLKNKKRQSDDTLCRFESVLDLKPSEPVGTGNSAPTQTSYQRRDTPT
LRSAAKQHYLKHSRYLPGISIRNGILSNPGKEFIPPNPWSSSGLSGKSSGTMSVISKVNS
VGSSSTSSSGLTGNYVPSFLKKEIGSAMQRVHLAPIPDPSPGYSSLKAMRPHPGRPFLDT
OPRSTPGLIPRPPAAQPVHGRTDWASKYPSRR

SEQ ID NO: 179\_AA839940\_M SSNNGGMSAEEEIGPGAEPMRGPSLATRDWRDETVGTTDLQQGIDPGAVSPEPGKDHAAQ GPGRTEAGRVSSAAEAAIVVLDDSAAPPAPFEHRVVSIKDTLISAGYTVSQHEVLGGGRF GQVHRCTERSTGLALAAKIIKVKNVKDREDVKNEVNIMNQLSHVNLIQLYDAFESKNSFT LIMEYVDGGELFDRITDEKYHLTELDVVLFTRQICEGVHYLHQHYILHLDLKPENILCVS

#### FIGURE 10

QTGHQIKIIDFGLARRYKPREKLKVNFGTPEFLAPEVVNYEFVSFPTDMWSVGVITYMLL SGLSPFLGETDAETMNFIVNCSWDFDADTFKGLSEEAKDFVSRLLVKEKSCRMSATQCLK HEWLNHLPAKASGSNVRLRSQQLLQKYMAQSKWKKHFHVVAAVNRLRKFPTCP

SEQ ID NO: 180\_AA460132\_H
MAAARATTPADGEEPAPEAEALAAARERSSRFLSGLELVKQGAEARVFRGRFQGRAAVIK
HRFPKGYRHPALEARLGRRRTVQEARALLRCRRAGISAPVVFFVDYASNCLYMEEIEGSV
TVRDYIQSTMETEKTPQGLSNLAKTIGQVLARMHDEDLIHGDLTTSNMLLKPPLEQLNIV
LIDFGLSFISALPEDKGVDLYVLEKAFLSTHPNTETVFEAFLKSYSTSSKKARPVLKKLD
EVRLRGRKRSMVG

SEQ ID NO: 181\_SGK034\_H
QREKVNQGNMPGLQSTFLAMDTEEGVEVVWNELHFGDRKAFAAHEEKIQTVFEQLVLVDH
PNIVKLHKYWLDTSEACARVIFITEYVSSGSLKQFLKKTKKNHKAMNARAWKRWCTQILS
ALSFLHACSPPIIHGNLTSDTIFIQHNGLIKIGSVWHRIFSNALPDDLRSPIRAEREELR
NLHFFPPEYGEVADGTAVDIFSFGMCALEMAVLEIQTNGDTRVTEEAIARARHSLSDPNM
REFILCCLARDPARRPSAHSLLFHRVLFEVHSLKLLAAHCFIQHQYLMPENVVEEKTKAM
DLHAVLAELPRPRRPPLQWRYSEVSFMELDKFLEDVRNGIYPLMNFAATRPLGLPRVLAP
PPEEVQKAKTPTPEPFDSETRKVIQMQCNLERSEDKARWHLTLLLVLEDRLHRQLTYDLL
PTDSAQDLASELVHYGFLHEDDRMKLAAFLESTFLKYRGTQA

SEQ ID NO: 182\_AA103218\_M SGK034\_M
HASAPEYGEVNDGTGFVDIFSFGMCALEMAVLEIQANGDTRVTEEAIARARHSLSDPNMR
EFILSCLARDPARRPSAHNLLFHRVLFEVHSLKLLAAHCFIQHQYLMPENVVEEKTKAMD
LHAVLAEMPQPHGPPMQWRYSEVSFLELDKFLEDVRNGIYPLMNFAAARPLGLPRVLAPP
PEEAQKAKTPTPEPFDSETRKVVQMQCNLERSEDKARWHLTLLLVLEDRLHRQLTYDLLP
TDSAQDLAAELVHYGFLHEDDRTKLAAFLETTFLKYRGTQA

SEQ ID NO: 183 NEK7 H, N34132 H MSGGAAEKQSSTPGSLFLSPPAPAPKNGSSSDSSVGEKLGAAAADAVTGRTEEYRRRRHT MDKDSRGAAATTTTTEHRFFRRSVICDSNATALELPGLPLSLPQPSIPAAVPQSAPPEPH REETVTATATSQVAQQPPAAAAPGEQAVAGPAPSTVPSSTSKDRPVSQPSLVGSKEEPPP ARSGSGGGSAKEPQEERSQQQDDIEELETKAVGMSNDGRFLKFDIEIGRGSFKTVYKGLD TETTVEVAWCELQDRKLTKSERQRFKEEAEMLKGLQHPNIVRFYDSWESTVKGKKCIVLV TELMTSGTLKTYLKRFKVMKIKVLRSWCRQILKGLQFLHTRTPLIIHRDLKCDNIFITGP TGSVKIGDLGLATLKRASFAKSVIGTPEFMAPEMYEEKYDESVDVYAFGMCMLEMATSEY PYSECQNAAQIYRRVTSGVKPASFDKVAIPEVKEIIEGCIRQNKDERYSIKDLLNHAFFQ EETGVRVELAEEDDGEKIAIKLWLRIEDIKKLKGKYKDNEAIEFCFDLERDVPEDVAQEM VESGYVCEGDHKTMAKAIKDRVSLIKRKREQRQLVREEQENKKQEESSLKQQVEQSSASQ TGIKQLPSASTGIPTASTTSASVSTQVEPEEPEADQHQQLQYQQPSISVLSDGTVDSGQG SSVFTESRVSSQQTVSYGFPXHEQAHSTGTVPGHIPSTVQAQSQPHGVYPPSSVQQGIQQ TAPPQQTVQYSLSQTSTSSEATTAQPVSQPQAPQVLPQVSAGKQSTQGVSQVAPAEPVAV AQPQATQPTTLASSVDSAHSDVASGMSDGNENVPSSSGRHEGRTTKRHYRKSVRSRSRHE KTSRPKLRILNVSNKGDRVVECQLETHNRKMVTFKFDLDGDNPEEIATIMVNNDFILAIE RESFVDQVREIIEKADEMLSEDVSVEPEGDQGLESLQGKDDYGFSGSQKLEGEFKQPIPA SSMPQQIGIPTSSLTQVVHSAGRRFIVSPVPESRLRESKVFPSEITDTVAASTAQSPGMN LSHSASSLSLQQAFSELRRAQMTEGPNTAPPNFSHTGPTFPVVPPFLSSIAGVPTTAAAT APVPATSSPPNDISTSVIQSEVTVPTEEGIAGVATSTGVVTSGGLPIPPVSESPVLSSVV SSITIPAVVSISTTSPSLQVPTSTSEIVVSSTALYPSVTVSATSASAGGSTATPGPKPPA VVSQQAAGSTTVGATLTSVSTTTSFPSTASQLSIQLSSSTSTPTLAETVVVSAHSLDKTS

#### FIGURE 1P

HSSTTGLAFSLSAPSSSSSPGAGVSSYISQPGGLHPLVIPSVIASTPILPQAAGPTSTPL
LPQVPSIPPLVQPVANVPAVQQTLIHSQPQPALLPNQPHTHCPEVDSDTQPKAPGIDDIK
TLEEKLRSLFSEHSSSGAQHASVSLETSLVIESTVTPGIPTTAVAPSKLLTSTTSTCLPP
TNLPLGTVALPVTPVVTPGQVSTPVSTTTSGVKPGTAPSKPPLTKAPVLPVGTELPAGTL
PSEQLPPFPGPSLTQSQQPLEDLDAQLRRTLSPEMITVTSAVGPVSMAAPTAITEAGTQP
QKGVSQVKEGPVLATSSGAGVFKMGRFQVSVAADGAQKEGKNKSEDAKSVHFESSTSESS
VLSSSSPESTLVKPEPNGITIPGISSDVPESAHKTTASEAKSDTGQPTKVGRFQVTTTAN
KVGRFSVSKTEDKITDTKKEGPVASPPFMDLEQAVLPAVIPKKEKPELSEPSHLNGPSSD
PEAAFLSRDVDDGSGSPHSPHQLSSKSLPSQNLSQSLSNSFNSSYMSSDNESDIEDEDLK
LELRRLRDKHLKEIQDLQSRQKHEIESLYTKLGKVPPAVIIPPAAPLSGRRRRPTKSKGS
KSSRSSSLGNKSPQLSGNLSGQSAASVLHPQQTLHPPGNIPESGQNQLLQPLKPSPSSDN
LYSAFTSDGAISVPSLSAPGQGNKATIIVQKQ

SEQ ID NO: 184\_BCON3\_H
MSEGESQTVLSSGSDPKVESSSSAPGLTSVSPPVTSTTSAASPEEEEESEDESEILEESP
CGRWQKRREEVNQRNVPGIDSAYLAMDTEEGVEVVWNEVQFSERKNYKLQEEKVRAVFDN
LIQLEHLNIVKFHKYWADIKENKARVIFITEYMSSGSLKQFLKKTKKNHKTMNEKAWKRW
CTQILSALSYLHSCDPPIIHGNLTCDTIFIQHNGLIKIGSVAPDTINNHVKTCREEQKNL
HFFAPEYGEVTNVTTAVDIYSFGMCALEMAVLEIQGNGESSYVPQEAISSAIQLLEDPLQ
REFIQKCLQSEPARRPTARELLFHPALFEVPSLKLLAAHCIVGHQHMIPENALEEITKNM
DTSAVLAEIPAGPGREPVQTLYSQSPALELDKFLEDVRNGIYPLTAFGLPRPQQPQQEEV
TSPVVPPSVKTPTPEPAEVETRKVVLMQCNIESVEEGVKHHLTLLLKLEDKLNRHLSCDL
MPNENIPELAAELVQLGFISEADQSRLTSLLEETLNKFNFARNSTLNSAAVTVSS

SEQ ID NO: 185\_AA711829\_M
LKQFLKKTKKNHKTMNEKAWKRWCTQILSALSYLHSCDPPIIHGNLTCDTIFIQHNGLIK
IGSVAPDTINNHVKTCREEQKNLHFFAPEYGEVTNVTTAVDIYSFGMCALEMAVLEIQGN
GESSYVPQEAISSAIQLLEDSLQREFIQKCLQSEPARRPTARELLFHPALFEVPSLKLLA
AHCIVGHQHMIPENALEEITKNMDTSAVLAEIPAGPGREPVQTLYSQSPALELDKFLEDV
RNGIYPLTAFGLPRPQQPQQEEVTSPVVPPSVKTPTPEPAEVETRKVVLMQCNIESVEEG
VKHHLTLLKLEDKLNRHLSCDLMPNESIPDLAAELVQLGFISEADQSRLTSLLEETLNK
FNFTRNSTLNTATVTVSS

SEQ ID NO: 186\_AA099102\_H
MSSCVSSQPSSNRAAPQDELGGRGSSSSESQKPCEALRGLSSLSIHLGMESFIVVTECEP
GCAVDLGLARDRPLEADGQEVPLDTSGSQARPHLSGRKLSLQERSQGGLAAGGSLDMNGR
CICPSLPYSPVSSPQSSPRLPRRPTVESHHVSITGMQDCVQLNQYTLKDEIGKGSYGVVK
LAYNENDNTYYAMKVLSKKKLIRQAAFPRRPPPRGTRPAPGGCIQPRGPIEQVYQEIAIL
KKLDHPNVVKLVEVLDDPNEDHLYMVFELVNQGPVMEVPTLKPLSEDQARFYFQDLIKGI
EYLHYQKIIHRDIKPSNLLVGEDGHIKIADFGVSNEFKGSDALLSNYVGTPAFMAPESLS
ETRKIFSGKAKDVWAMGVTLYCFVFGQCPFMDERIMCLHSKIKSQALEFPDQPDIAEDLK
DLITRMLDKNPESRIVVPEIKLHPWVTRHGAEPLPSEDENCTLVEVTEEEVENSVKHIPS
LATVILVKTMIRKRSFGNPFEGSRREERSLSAPGNLLTKKPTRECESLSELKEARQRRQP
PGHRPAPRGGGGSALVRGSPCVESCWAPAPGSPARMHPLRPEEAMEPE

SEQ ID NO: 187\_5R69\_17\_2\_H MQEIPQEQIKEIKKEQLSGSPWILLRENEVSTLYKGEYHRAPVAIKVFKKLQAGSIAIVR QTFNKEIKTMKKFESPNILRIFGICIDETVTPPQFSIVMEYCELGTLRELLDREKDLTLG

#### FIGURE 1Q

KRMVLVLGAARGLYRLHHSEAPELHGKIRSSNFLVTQGYQVKLAGFELRKTQTSMSLGTT REKTDRVKSTAYLSPQELEDVFYQYDVKSEIYSFGIVLWEIATGDIPFQGEECEDWLSQW

SEQ ID NO: 188 H85811 H MAPVYEGMASHVQVFSPHTLQSSAFCSVKKLKIEPSSNWDMTGYGSHSKVYSQSKNIPLS QPATTTVSTSLPVPNPSLPYEQTIVFPGSTGHIVVTSASSTSVTGQVLGGPHNLMRRSTV SLLDTYQKCGLKRKSEEIENTSSVQIIEEHPPMIQNNASGATVATATTSTATSKNSGSNS EGDYQLVQHEVLCSMTNTYEVLEFLGRGTFGQVVKCWKRGTNEIVAIKILKNHPSYARQG QIEVSILARLSTESADDYNFVRAYECFQHKNHTCLVFEMLEQNLYDFLKQNKFSPLPLKY IRPVLQQVATALMKLKSLGLIHADLKPENIMLVDPSRQPYRVKVIDFGSASHVSKAVCST YLQSRYYRAPEIILGLPFCEAIDMWSLGCVIAELFLGWPLYPGDSEYDQIRYISQTQGLP AEYLLSAGTKTTRFFNRDTDSPYPLWRLKTPDDHEAETGIKSKEARKYIFNCLDDMAQVN MTTDLEGSDMLVEKADRREFIDLLKKMLTIDADKRITPIETLNHPFVTMTHLLDFPHSTH VKSCFQNMEICKRRVNMYDTVNQSKTPFITHVAPSTSTNLTMTFNNQLTTVHNQPSAASM AAVAQRSMPLQTGTAQICARPDPFQQALIVCPPGFQGLQASPSKHAGYSVRMENAVPIVT QAPGAQPLQIQPGLLAQQAWPSGTQQILLPPAWQQLTGVATHTSVQHATVIPETMAGTQQ LADWRNTHAHGSHYNPIMQQPALLTGHVTLPAAQPLNVGVAHVMRQQPTSTTSSRKSKQH QSSVRNVSTCEVSSSQAISSPQRSKRVKENTPPRCAMVHSSPACSTSVTCGWGDVASSTT RERQRQTIVIPDTPSPTVSVITISSDTDEEEEQKHAPTSTVSKQRKNVISCVTVHDSPYS DSSSNTSPYSVQQRAGHNNANAFDTKGSLENHCTGNPRTIIVPPLKTQASEVLVECDSLV PVNTSHHSSSYKSKSSSNVTSTSGHSSGSSSGAITYRQQRPGPHFQQQQPLNLSQAQQHI TTDRTGSHRRQQAYITPTMAQAPYSFPHNSPSHGTVHPHLAAAAAAAHLPTQPHLYTYTA PAALGSTGTVAHLVASQGSARHTVQHTAYPASIVHQVPVSMGPRVLPSPTIHPSQYPAQF AHQTYISASPASTVYTGYPLSPAKVNQYPYI

SEQ ID NO: 189\_DYRK3\_H
MMIDETKCPPCSNVLCNPSEPPPPRRLNMTAEQFTGDHTQHFLDGGEMKVEQLFQEFGNR
KSNTIQSDGISDSEKCSPTVSQGKSSDCLNTVKSNSSSKAPKVVPLTPEQALKQYKHHLT
AYEKLEIINYPEIYFVGPNAKKRHGVIGGPNNGGYDDADGAYIHVPRDHLAYRYEVLKII
GKGSFGQVARVYDHKLRQYVALKMVRNEKRFHRQAAEEIRILEHLKKQDKTGSMNVIHML
ESFTFRNHVCMAFELLSIDLYELIKKNKFQGFSVQLVRKFAQSILQSLDALHKNKIIHCD
LKPENILLKHHGRSSTKVIDFGSSCFEYQKLYTYIQSRFYRAPEIILGSRYSTPIDIWSF
RCILAELLTGQPLFPGEDEGDQLACMMELLGMPPPKLLEQSKRAKYFINSKGIPRYCSVT
TQADGRVVLVGGRSRRGKKRGPPGSKDWGTALKGCDDYLFIEFLKRCLHWDPSARLTPAQ
ALRHPWISKSVPRPLTTIDKVSGKRVVNPASAFQGLGSKLPPVVGIANKLKANLMSETNG
SIPLCSVLPKLIS

SEQ ID NO: 190\_AA589241\_M DYRK3\_M
TRPELLGMPPQKLLEQSKRAKYFINSKGLPRYCSVSTQTDGRVVLLGGRSRRGKKRGPPG
SKDWATALKGCGDYLFIEFLKRCLQWDPSARLTPAQALRHPWISKSTPKPLTMDKVPGKR
VVNPTNAFQGLGSKLPPVVGIASKLKANLMSETSGSIPLCSVLPKLIS

SEQ ID NO: 191\_5R72\_16\_2\_H
MAGGRGAPGRGRDEPPESYPQRQDHELQALEAIYGADFQDLRPDACGPVKEPPEINLVLY
PQGLTGEEVYVKVDLRVKCPPTYPDVVPEIELKNAKGLSNESVNLLKSRLEELAKKHCGE
VMIFELAYHVQSFLSEHNKPPPKSFHEEMLERRAQEEQQRLLEAKRKEEQEQREILHEIQ
RRKEEIKEEKKRKEMAKQERLEIASLSNQDHTSKKDPGGHRTAAILHGGSPDFVGNGKHR
ANSSGRSRRERQYSVCNSEDSPGSCEILYFNMGSPDQLMVHKGKCIGSDEQLGKLVYNAL
ETATGGFVLLYEWVLQWQKKMGPFLTSQEKEKIDKCKKQIQGTETEFNSLVKLSHPNVVR

#### FIGURE 1R

YLAMNLKEQDDSIVVDILVEHISGVSLAAHLSHSGPIPVHQLRRYTAQLLSGLDYLHSNS VVHKVLSASNVLVDAEGTVKITDYSISKRLADICKEDVFEQTRVRFSDNALPYKTGKKGD VWRLGLLLLSLSQGQECGEYPVTIPSDLPADFQDFLKKCVCLDDKERWSPQQLLKHSFIN POPKMPLVEOSPEDSGGODYVETVIPSNRLPSAAFFSETOROFSRYFIEFEELQLLGKGA FGAVIKVONKLDGCCYAVKRIPINPASRQFRRIKGEVTLLSRLHHENIVRYYNAWIERHE RPAGPGTPPPDSGPLAKDDRAARGQPASDTDGLDSVEAAAPPPILSSSVEWSTSGERSAS ARFPATGPGSSDDEDDDEDEHGGVFSQSFLPASDSESDIIFDNEDENSKSQNQDEDCNEK NGCHESEPSVTTEAVHYLYIQMEYCEKSTLRDTIDQGLYRDTVRLWRLFREILDGLAYIH EKGMIHRDLKPVNIFLDSDDHVKIGDFGLATDHLAFSADSKQDDQTGDLIKSDPSGHLTG MVGTALYVSPEVQGSTKSAYNQKVDLFSLGIIFFEMSYHPMVTASERIFVLNQLRDPTSP KFPEDFDDGEHAKQKSVISWLLNHDPAKRPTATELLKSELLPPPQMEESELHEVLHHTLT NVDGKAYRTMMAQIFSQRISPAIDYTYDSDILKGNFSIRTAKMQQHVCETIIRIFKRHGA VQLCTPLLLPRNRQIYEHNEAALFMDHSGMLVMLPFDLRIPFARYVARNNILNLKRYCIE RVFRPRKLDRFHPKELLECAFDIVTSTTNSFLPTAEIIYTIYEIIQEFPALQERNYSIYL NHTMLLKAILLHCGIPEDKLSQVYIILYDAVTEKLTRREVEAKFCNLSLSSNSLCRLYKF IEQKGDLQDLMPTINSLIKQKTGIAQLVKYGLKDLEEVVGLLKKLGIKLQVLINLGLVYK VOOHNGIIFQFVAFIKRRQRAVPEILAAGGRYDLLIPQFRGPQALGPVPTAIGVSIAIDK ISAAVLNMEESVTISSCDLLVVSVGQMSMSRAINLTQKLWTAGITAEIMYDWSQSQEELQ EYCRHHEITYVALVSDKEGSHVKVKSFEKERQTEKRVLETELVDHVLQKLRTKVTDERNG REASDNLAVONLKGSFSNASGLFEIHGATVVPIVSVLAPEKLSASTRRRYETQVQTRLQT SLANLHQKSSEIEILAVDLPKETILQFLSLEWDADEQAFNTTVKQLLSRLPKQRYLKLVC DEIYNIKVEKKVSVLFLYSYRDDYYRILF

SEQ ID NO: 192\_R43524\_H, HRI\_H
MLGGNSGVRKREEEGDGAGAVAAPPAIDFPAEGPDPEYDESDVPAEIQVLKEPLQQPTFP
FAVANQLLLVSLLEHLSHVHEPNPLRSRQVFKLLCQTFIKMGLLSSFTCSDEFSSLRLHH
NRAITHLMRSAKERVRQDPCEDISRIQKIRSREVALEAQTSRYLNEFEELVILGKGGYGR
VYKVRNKLDGQYYAIKKILIKGATKTVCMKVLREVKVLAGLQHPNIVGYHTAWIEHVHVI
QPRADRAAIELPSLEVLSDQEEDREQCGVKNDESSSSSIIFAEPTPEKEKRFGESDTENQ
NNKSVKYTTNLVIRESGELESTLELQENGLAGLSASSIVEQQLPLRRNSHLEESFTSTEE
SSEENVNFLGQTEAQYHLMLHIQMQLCELSLWDWIVERNKRGREYVDESACPYVMANVAT
KIFQELVEGVFYIHNMGIVHRDLKPRNIFLHGPDQQVKIGDFGLACTDILQKNTDWTNRN
GKRTPTHTSRVGTCLYASPEQLEGSEYDAKSDMYSLGVVLLELFQPFGTEMERAEVLTGL
RTGQLPESLRKRCPVQAKYIQHLTRRNSSQRPSAIQLLQSELFQNSGNVNLTLQMKIIEQ
EKEIAELKKQLNLLSQDKGVRDDGKDGGVG

SEQ ID NO: 193\_17000057519457\_H
MAAARATTPADGEEPAPEAEALAAARERSSRFLSGLELVKQGAEARVFRGRFQGRAAVIK
HRFPKGYRHPALEARLGRRRTVQEARALLRCRRAGISAPVVFFVDYASNCLYMEEIEGSV
TVRDYIQSTMETEKTPQGLSNLAKTIGQVLARMHDEDLIHGDLTTSNMLLKPPLEQLNIV
LIDFGLSFISALPEDKGVDLYVLEKAFLSTHPNTETVFEAFLKSYSTSSKKARPVLKKLD
EVRLRGRKRSMVG

SEQ ID NO: 194\_AA013524\_M LVQQGAEARVFRGRFQGRAAVVKHRFPKSYRHPELEARLGRRRTVQEARALLRCRRAGIA APVVFFVDYASNCLYMEEIEDSVTVRDYIQSTMETEKDPQCLLDLARRMGQVLAGMHDQD LIHGDLTTSNMLLRRPLAQLHIVLIDFGLSFVSGLPEDKGVDLYVLEKAFLSTHPHTETA FEAFLKSYGASSKKSSPVLKKLDEVRLRGRKRSMVG

## FIGURE 1S

SEQ ID NO: 195\_17000139801197\_H, IRAKM\_H
MAGNCGARGALSAHTLLFDLPPALLGELCAVLDSCDGALGWRGLAERLSSSWLDVRHIEK
YVDQGKSGTRELLWSWAQKNKTIGDLLQVLQEMGHRRAIHLITNYGAVLSPSEKSYQEGG
FPNILFKETANVTVDNVLIPEHNEKGVLLKSSISFQNIIEGTRNFHKDFLIGEGEIFEVY
RVEIQNLTYAVKLFKQEKKMQCKKHWKRFLSELEVLLLFHHPNILELAAYFTETEKFCLI
YPYMRNGTLFDRLQCVGDTAPLPWHIRIGILIGISKAIHYLHNVQPCSVICGSISSANIL
LDDQFQPKLTDFAMAHFRSHLEHQSCTINMTSSSSKHLWYMPEEYIRQGKLSIKTDVYSF
GIVIMEVLTGCRVVLDDPKHIQLRDLLRELMEKRGLDSCLSFLDKKVPPCPRNFSAKLFC
LAGRCAATRAKLRPSMDEVLNTLESTQASLYFAEDPPTSLKSFRCPSPLFLENVPSIPVE
DDESQNNNLLPSDEGLRIDRMTQKTPFECSQSEVMFLSLDKKPESKRNEEACNMPSSSCE
ESWFPKYIVPSQDLRPYKVNIDPSSEAPGHSCRSRPVESSCSSKFSWDEYEQYKKE

SEQ ID NO: 196\_AA840598\_M IRAKM\_M
MWKRFLSELEVLLLFRHPHILELAAYFTETEKLCLVYPYMSNGTLFDRLQCTNGTTPLSW
HVRISVLIGIAKAIQYLHNTQPCAVICGNVSSANILLDDQLQPKLTDFAAAHFRPNLEQQ
SSTINMTGGGRKHLWYMPEEYIRQGRLSVKTDVYSFGIVIMEVLTGCKVVLDDPKHVQLR
DLLMELMEKRGLDSCLSFLDRKIPPCPRNFSAKLFSLAGRCVATKAKLRPTMDEVLSSLE
STQPSLYFAEDPPTSLKSFRCPSPLFLDNVPSIPVEDDENQNNHSVPPKEVLGTDRVTQK
TPFECSQSEVTFLGLDRNRGNRGSEADCNVPSSSHEECWSPELVAPSQDLSPTVISLGSS
WEVPGHSYGSKPMEKRCSSGLFCSEHEQSKKQ

SEQ ID NO: 197 AA088547 H MASAVRGSRPWPRLGLQLQFAALLLGTLSPQVHTLRPENLLLVSTLDGSLHALSKQTGDL KWTLRDDPVIEGPMYVTEMAFLSDPADGSLYILGTQKQQGLMKLPFTIPELVHASPCRSS DGVFYTGRKQDAWFVVDPESGETQMTLTTEGPSTPRLYIGRTQYTVTMHDPRAPALRWNT TYRRYSAPPMDGSPGKYMSHLASCGMGLLLTVDPGSGTVLWTQDLGVPVMGVYTWHQDGL RQLPHLTLARDTLHFLALRWGHIRLPASGPRDTATLFSTLDTQLLMTLYVGKDETGFYVS KALVHTGVALVPRGLTLAPADGPTTDEVTLQVSGEREGSPSTAVRYPSGSVALPSQWLLI GHHELPPVLHTTMLRVHPTLGSGTAETRPPENTQAPAFFLELLSLSREKLWDSELHPEEK TPDSYLGLGPQDLLAASLTAVLLGGWILFVMRQVVEKQQETPLAPADFAHISQDAQSLHS GASRRSQKRLQSPSKQAQPLDDPEAEQLTVVGKISFNPKDVLGRGAGGTFVFRGQFEGRA VAVKRLLRECFGLVRREVQLLQESDRHPNVLRYFCTERGPQFHYIALELCRASLQEYVEN PDLDRGGLEPEVVLQQLMSGLAHLHSLHIVHRDLKPGNILITGPDSQGLGRVVLSDFGLC KKLPAGRCSFSLHSGIPGTEGWMAPELLQLLPPDSPTSAVDIFSAGCVFYYVLSGGSHPF GDSLYRQANILTGAPCLAHLEEEVHDKVVARDLVGAMLSPLPQPRPSAPQVLAHPFFWSR AKQLQFFQDVSDWLEKESEQEPLVRALEAGGCAVVRDNWHEHISMPLQTDLRKFRSYKGT SVRDLLRAVRNKKHHYRELPVEVRQALGQVPDGFVQYFTNRFPRLLLHTHRAMRSCASES LFLPYYPPDSEARRPCPGATGR

SEQ ID NO: 198\_HGP\_66444466
MEGISNFKTPSKLSEKKKSVLCSTPTINIPASPFMQKLGFGTGVNVYLMKRSPRGLSHSP
WAVKKINPICNDHYRSVYQKRLMDEAKILKSLHHPNIVGYRAFTEANDGSLCLAMEYGGE
KSLNDLIEERYKASQDPFPAAIILKVALNMARGLKYLHQEKKLLHGDIKSSNVVIKGDFE
TIKICDVGVSLPLDENMTVTDPEACYIGTEPWKPKEAVEENGVITDKADIFAFGLTLWEM
MTLSIPHINLSNDDDDDEDKTFDESDFDDEAYYAALGTRPPINMEELDESYQKVIELFSVC
TNEDPKDRPSAAHIVEALETDV

SEQ ID NO: 199\_AA449542\_M SPRGLSHSPWAVKKISLLCDDHYRTVYQKRLTDEAKILKNLNHPNIIGYRAFTEASDGSL CLAMEYGGEKSLNDLIEERNKDSGSPFPAAVILRVALHMARGLKYLHQEKKLLHGDIKSS

#### FIGURE 1T

NVVIKGDFETIKICDVGVSLPLDENMTVTDPEACYIGTEPWKPKEALEENGIITDKADVF AFGLTLWEMMTLCIPHVNLPDDDVDEDATFDESDFDDEAYYAALGTRPSINMELDDSYQK AIELFCVCTNEDPKDRPSAAHIVEALELDGQCCGLSESKH

SEQ ID NO: 200\_5R57\_10\_2\_M TESK2\_M LLDSDLYLPWTVRVKLAYGIAVGLSYLHFKGIFHRDLTSKV

SPAKTNKERARGDHRGWRNF

SEQ ID NO: 201\_AA232253\_H

MSSLGASFVQIKFDDLQFFENCGGGSFGSVYRAKWISQDKEVAVKKLLKIEKEAEILSVL
SHRNIIQFYGVILEPPNYGIVTEYASLGSLYDYINSNRSEEMDMDHIMTWATDVAKGMHY
LHMEAPVKVIHRDLKSRNVVIAADGVLKICDFGASRFHNHTTHMSLVGTFPWMAPEVIQS
LPVSETCDTYSYGVVLWEMLTREVPFKGLEGLQVAWLVVEKNERLTIPSSCPRSFAELLH
QCWEADAKKRPSFKQIISILESMSNDTSLPDKCNSFLHNKAEWRCEIEATLERLKKLERD
LSFKEQELKERERRLKMWEQKLTEQSNTPLLPSFEIGAWTEDDVYCWVQQLVRKGDSSAE
MSVYASLFKENNITGKRLLLLEEEDLKDMGIVSKGHIIHFKSAIEKLTHDYINLFHFPPL
IKDSGGEPEENEEKIVNLELVFGFHLKPGTGPQDCKWKMYMEMDGDEIAITYIKDVTFNT
NLPDAEILKMTKPPFVMEKWIVGIAKSQTVECTVTYESDVRTPKSTKHVHLIQWSRTKPQ
DEVKAVQLAIQTLFTNSDGNPGSRSDSSADCQWLDTLRMRQIASNTSLQRSQSNPILGSP
FFSHFDGQDSYAAAVRRPQVPIKYQQITPVNQSRSSSPTQYGLTKNFSSLHLNSRDSGFS
SGNTDTSSERGRYSDRSRNKYGRGSISLNSSPRGRYSGKSQHSTPSRGRYPGKFYRVSQS
ALNPHOSPDFKRSPRDLHQPNTIPGMPLHPETDSRASEEDSKVSEGGWTKVEYRKKPHRP

SEQ ID NO: 202\_AI375137\_H

MGNYKSRPTQTCTDEWKKKVSESYVITIERLEDDLQIKEKELTELRNIFGSDEAFSKVNL
NYRTENGLSLLHLCCICGGKKSHIRTLMLKGLRPSRLTRNGFTALHLAVYKDNAELITSL
LHSGADIQQVGYGGLTALHIATIAGHLEAADVLLQHGANVNIQDAVFFTPLHIAAYYGHE
QVTRLLLKFGADVNVSGEVGDRPLHLASAKGFLNIAKLLMEEGSKADVNAQDNEDHVPLH
FCSRFGHHDIVKYLLQSDLEVQPHVVNIYGDTPLHLACYNGKFEVAKEIIQISGTESLTK
ENIFSETAFHSACTYGKSIDLVKFLLDQNVININHQGRDGHTGLHSACYHGHIRLVQFLL
DNGADMNLVACDPSRSSGEKDEQTCLMWAYEKGHDAIVTLLKHYKRPQDELPCNEYSQPG
GDGSYVSVPSPLGKIKSMTKEKADILLLRAGLPSHFHLQLSEIEFHEIIGSGSFGKVYKG
RCRNKIVAIKRYRANTYCSKSDVDMFCREVSILCQLNHPCVIQFVGACLNDPSQFAIVTQ
YISGGSLFSLLHEQKRILDLQSKLIIAVDVAKGMEYLHNLTQPIIHRDLNSHNILLYEDG
HAVVADFGESRFLQSLDEDNMTKQPGNLRWMAPEVFTQCTRYTIKADVFSYALCLWEILT
GEIPFAHLKPAAAAADMAYHHIRPPIGYSIPKPISSLLIRGWNACPEGRPEFSEVVMKLE
ECLCNIELMSPASSNSSGSLSPSSSSDCLVNRGGPGRSHVAALRSRFELEYALNARSYAA
LSQSAGQYSSQGLSLEEMKRSLQYTPIDKYGYVSDPMSSMHFHSCRNSSSFEDSS

SEQ ID NO: 203\_H97685\_H
MESERSPLYRQLIDLGYLSSSHWNCGAPGQDTKAQSMLVEQSEKLRHLSTFSHQVLQTRL
VDAAKALNLVHCHCLDIFINQAFDMQRDLQITPKRLEYTRKKENELYESLMNIANRKQEE
MKDMIVETLNTMKEELLDDATNMEFKDVIVPENGEPVGTREIKCCIRQIQELIISRLNQA
VANKLISSVDYLRESFVGTLERCLQSLEKSQDVSVHITSNYLKQILNAAYHVEVTFHSGS
SVTRMLWEQIKQIIQRITWVSPPAITLEWKRKVAQEAIESLSASKLAKSICSQFRTRLNS
SHEAFAASLRQLEAGHSGRLEKTEDLWLRVRKDHAPRLARLSLESRSLQDVLLHRKPKLG
QELGRGQYGVVYLCDNWGGHFPCALKSVVPPDEKHWNDLALEFHYMRSLPKHERLVDLHG
SVIDYNYGGGSSIAVLLIMERLHRDLYTGLKAGLTLETRLQIALDVVEGIRFLHSQGLVH
RDIKLKNVLLDKQNRAKITDLGFCKPEAMMSGSIVGTPIHMAPELFTGKYDNSVDVYAFG

#### FIGURE 1U

ILFWYICSGSVKLPEAFERCASKDHLWNNVRRGARPERLPVFDEECWQLMEACWDGDPLK RPLLGIVQPMLQGIMNRLCKSNSEQPNRGLDDST

SEQ ID NO: 204\_W20810\_M
DVNLKASKASDVYSFGILVWAVLAGREAELVDKTSLIRETVCDRQSRPPLTELPPGSPET
PGLEKLKELMIHCWGSQSENRPSFQDCEPKTNEVYNLVKDKVDAAVSEVKHYLSQHRSSG
RNLSAREPSQRGTEMDCPRETMVSKMLDRLHLEEPSGPVPGKCPERQAQDTSVGPATPAR
TSSDPVAGTPQIPHTLPFRGTTPGPVFTETPGPHPQRNQGDGRHGTPWYPWTPPNPMTGP
PALVFNNCSEVQIGNYNSLVAPPRTTASSSAKYDQAQFGRGRGWQPFHK

SEQ ID NO: 205\_AA744236\_H

MGSENSALKSYTLREPPFTLPSGLAVYPAVLQDGKFASVFVYKRENEDKVNKAAKHLKTL
RHPCLLRFLSCTVEADGIHLVTERVQPLEVALETLSSAEVCAGIYDILLALIFLHDRGHL
THNNVCLSSVFVSEDGHWKLGGMETVCKVSQATPEFLRSIQSIRDPASIPPEEMSPEFTT
LPECHGHARDAFSFGTLVESLLTILNEQVSADVLSSFQQTLHSTLLNPIPKCRPALCTLL
SHDFFRNDFLEVVNFLKSLTLKSEEEKTEFFKFLLDRVSCLSEELIASRLVPLLLNQLVF
AEPVAVKSFLPYLLGPKKDHAQGETPCLLSPALFQSRVIPVLLQLFEVHEEHVRMVLLSH
IEAYVEHFTQEQLKKVILPQVLLGLRDTSDSIVAITLHSLAVLVSLLGPEVVVGGERTKI
FKRTAPSFTKNTDLSLEGDPFSQPIKFPINGLSDVKNTSEDSENFPSSSKKSEEWPDWSE
PEEPENQTVNIQIWPREPCDDVKSQCTTLDVEESSWDDCEPSSLDTKVNPGGGITATKPV
TSGEQKPIPALLSLTEESMPWKSSLPQKISLVQRGDDADQIEPPKVSSQERPLKVPSELG
LGEEFTIQVKKKPVKDPEMDWFADMIPEIKPSAAFLILPELRTEMVPKKDDVSPVMQFSS
KFAAAEITEGEAEGWEEEGELNWEDNNW

SEQ ID NO: 206\_A1052250\_H

MESMLNKLKSTVTKVTADVTSAVMGIPVTREFDVGRHIASGCNGLAWKIFNGTKKSTKQE
VAVFVFDKKLIDKYQKFEKDQIIDSLKRGVQQLTRLRHPRLLTVQHPLEESRDCLAFCTE
PVFASLANVLGNWENLPSPISPDIKDYKLYDVETKYGLLQVSEGLSFLHSSVKMVHGNIT
PENIILNKSGAWKIMGFDFCVSSTNPSEQEPKFPCKEWDPNLPSLCLPNPEYLAPEYILS
VSCETASDMYSLGTVMYAVFNKGKPIFEVNKQDIYKSFSRQLDQLSRLGSSSLTNIPEEV
REHVKLLLNVTPTVRPDADQMTKIPFFDDVGAVTLQYFDTLFQRDNLQKSQFFKGLPKVL
PKLPKRVIVQRILPCLTSEFVNPDMVPFVLPNVLLIAEECTKEEYVKLILPELGPVFKQQ
EPIQILLIFLQKMDLLLTKTPPDEIKNSVLPMVYRALEAPSIQIQELCLNIIPTFANLID
YPSMKNALIPRIKNACYKHLPLRFV

SEQ ID NO: 207\_AA278842\_H

MWFFARDPVRDFPFELIPEPPEGGLPGPWALHRGRKKATGSPVSIFVYDVKPGAEEQTQV

AKAAFKRFKTLRHPNILAYIDGLETEKCLHVVTEAVTPLGIYLKARVEAGGLKELEISWG

LHQIVKALSFLVNDCSLIHNNVCMAAVFVDRAGEWKLGGLDYMYSAQGNGGGPPRKGIPE

LEQYDPPELADSSGRVVREKWSADMWRLGCLIWEVFNGPLPRAAALRNPGKIPKTLVPHY

CELVGANPKVRPNPARFLQNCRAPGGFMSNRFVETNLFLEEIQIKEPAEKQKFFQELSKS

LDAFPEDFCRHKVLPQLLTAFEFGNAGAVVLTPLFKVGKFLSAEEYQQKIIPVVVKMFSS

TDRAMRIRLLQQMEQFIQYLDEPTVNTQIFPHVVHGFLDTNPAIREQTVKSMLLLAPKLN

EANLNVELMKHFARLQAKDEQGPIRCNTTVCLGKIGSYLSASTRHRVLTSAFSRATRDPF

APSRVAGVLGFAATHNLYSMNDCAQKILPVLCGLTVDPEKSVRDQAFKAIRSFLSKLESV

SEDPTQLEEVEKDVHAASSPGMGGAAASWAGWAVTGVSSLTSKLIRSHPTTAPTETNIPQ

RPTPEGVPAPAPTPVPATPTTSGHWETQEEDKDTAEDSSTADRWDDEDWGSLEQEAESVL

AQQDDWSTGGQVSRASQVSNSDHKSSKSPESDWSSWEAEGSWEQGWQEPSSQEPPPDGTR

LASEYNWGGPESSDKGDPFATLSARPSTQPRPDSWGEDNWEGLETDSRQVKAELARKKRE

ERRREMEAKRAERKVAKGPMKLGARKLD

#### FIGURE 1V

SEQ ID NO: 208\_AA599286\_H

MAFMEKPPAGKVLLDDTVPLTAAIEASQSLQSHTEYIIRVQGGISVENSWQIVRRYSDFD

LLNNSLQIAGLSLPLPPKKLIGNMDREFIAERQKGLQNYLNVITTNHILSNCELVKKFLD

PNNYSANYTEIALQQVSMFFRSEPKWEVVEPLKDIGWRIRKKYFLMKIKNQPKERLVLSW

ADLGPDKYLSDKDFQCLIKLLPSCLHPYIYRVTFATANESSALLIRMFNEKGTLKDLIYK

AKPKDPFLKKYCNPKKIQGLELQQIKTYGRQILEVLKFLHDKGFPYGHLHASNVMLDGDT

CRLLDLENSLLGLPSFYRSYFSQFRKINTLESVDVHCFGHLLYEMTYGRPPDSVPVDSFP

PAPSMAVVAVLESTLSCEACKNGMPTISRLLQMPLFSDVLLTTSEKPQFKIPTKLKEALR

IAKECIEKRLIEEQKQIHQHRRLTRAQSHHGSEEERKKRKILARKKSKRSALENSEEHSA

KYSNSNNSAGSGASSPLTSPSSPTPPSTSGISALPPPPPPPPPPPAAPLPPASTEAPAQLS

SQAVNGMSRGALLSSIQNFQKGTLRKAKPVITVLRRSAEASCLHLEGKVLFYSYSPLPPN

YPLPGKVIAEPVQPQTVLFCRCSCKQLFERNNSLSRIKLGWHAKKKKKK

SEQ ID NO: 209\_AA425725\_H

MSASTGGGGDSGGSGSSSSQASCGPESSGSELALATPVPQMLQGLLGSDDEEQEDPKD
YCKGGYHPVKIGDVFNGRYHVVRKLGWGHFSTVWLCWDIQRKRFVALKVVKSAGHYTETA
VDEIKLLKCVRDSDPSDPKRETIVQLIDDFRISGVNGVHVCMVLEVLGHQLLKWIIKSNY
QGLPVPCVKSIVRQVLHGLDYLHTKCKIIHTDIKPENILLCVGDAYIRRLAAEATEWQQA
GAPPPSRSIVSTAPQEVLTGKLSKNKRKKMRRKRKQQKRLLEERLRDLQRLEAMEAATQA
EDSGLRLDGGSGSTSSSGFSGSLFSPASCSILSGSSNQRETGGLLSPSTPFGASNLLVNP
LEPQNADKIKIKIADLGNACWVHKHFTEDIQTRQYRAVEVLIGAEYGPPADIWSTACMAF
ELATGDYLFEPHSGEDYSRDEDHIAHIVELLGDIPPAFALSGRYSREFFNRRGELRHIHN
LKHWGLYEVLMEKYEWPLEQATQFSAFLLPMMEYIPEKRASAADCLQHPWLNP

SEQ ID NO: 210\_SGK022\_H
MEDFLLSNGYQLGKTIGEGTYSKVKEAFSKKHQRKVAIKVIDKMGGPSEFIQRFLPRELQ
IVRTLDHKNIIQVYEMLESADGKICLVMELAEGGDVFDCVLNGGPLPESRAKALFRQMVE
AIRYCHGCGVAHRDLKCENALLQGFNLKLTDFGFAKVLPKSHRELSQTFCGSTAYAAPEV
LQGIPHDSKKGDVWSMGVVLYVMLCASLPFDDTDIPKMLWQQQKGVSFPTHLSISADCQD
LLKRLLEPDMILRPSIEEVSWHPWLAST

SEQ ID NO: 211\_AA060026\_M SGK022\_M
MEDFLLSNGYQLGKTIGEGTYSKVKEAFSKKHQRKVAIKIIDKMGGPEEFIQRFLPRELQ
IVRTLDHKNIIQVYEMLESADGKIYLVMELAEGGDVFDCVLNGGPLPESRAKALFRQMVE
AIRYCHGCGVAHRDLKCENALLQGFNLKLTDFGFAKVLPKSRRELSQTFCGSTAYAAPEV
LQGIPHDSKKGDVWSMGVVLYVMLCASLPFDDTDIPKMLWQQQKGVSFPTHLGISTECQD
LLKRLLEPDMILRPSIEEVSWHPWLAST

SEQ ID NO: 212\_AA399669\_H
MGKGDVLEAAPTTTAYHSLMDEYGYEVGKAIGHGSYGSVYEAFYTKQKVMVAVKIISKKK
ASDDYLNKFLPREIQQVMKVLRHKYLINFYRAIESTSRVYIILELAQGGDVLEWIQRYGA
CSEPLAGKWFSQLTLGIAYLHSKSIVHRDLKLENLLLDKWENVKISDFGFAKMVPSNQPV
GCSPXYRQVNCFSHLSQTYCGSFAYACPEILRGLPYNPFLSDTWSMGVILYTLVVAHLPF
DDTNLKKLLRETOKEVTFPANHTISQECKVQLLIACVAQWRKTQARPLSPLL

SEQ ID NO: 213\_AA758539\_H MDDATVLRKKGYIVGINLGKGSYAKVKSAYSERLKFNVAVKIIDRRKTPTDFVERFLPRE MDILATVNHGSIIKTYEIFETSDGRIYIIMELGVQGDLLEFIKCQGALHEDVARKMFRQL SSAVKYCHDLDIVHRDLKCENLLLDKDFNIKLSDFGFSKRCLRDSNGRIILSKTFCGSAA

24/1/3

### FIGURE 1W

YAAPEVLQSIPYQPKVYDIWSLGVILYIMVCGSMPYDDSDIRKMLRIQKEHRVDFPRSKN LTCECKDLIYRMLQPDVSQRLHIDEILSHSWLQPPKPKATSSASFKREGEGKYRAECKLD TKTGLRPDHRPDHKLGAKTQHRLLVVPENENRMEDRLAETSRAKDHHISGAEVGKAST

SEQ ID NO: 214\_AA883975\_H
MSGDKLLSELGYKLGRTIGEGSYSKVKVATSKKYKGTVAIKVVDRRRAPPDFVNKFLPRE
LSILRGVRHPHIVHVFEFIEVCNGKLYIVMEAAATDLLQAVQRNGRIPGVQARDLFAQIA
GAVRYLHDHHLVHRDLKCENVLLSPDERRVKLTDFGFGRQAHGYPDLSTTYCGSAAYASP
EVLLGIPYDPKKYDVWSMGVVLYVMVTGCMPFDDSDIAGLPRRQKRGVLYPEGLELSERC
KALIAELLQFSPSARPSAGQVARNCWLRAGDSG

SEQ ID NO: 215\_AA905446\_H VGRQETGVRRWAFLICQPISPPLTSSEFIQRFLPRELQIVRTLDHKNIIQVYEMLESADG KICLVMELAEGGDVFDCVLNGGPLPESRAKALFRQMVEAIRYCHGCGVAHRDLKCENALL QGFNLKLTDFGFAKVLPKSHRELSQTFCGSTAYAAPEVLQGIPXKMLWQQQKGVSFPTHL SISADCQDLLKRLLEPDMILRPSIEEVSWHPWLAST

SEQ ID NO: 216\_H29974\_H
YSLLAEIGRGSYGVVYEAVAGRSGARVAVKKIRCDAPENVELALAEFWALTSLKRRHQNV
VQFEECVLQRNGLAQRMSHGNKSSQLYLRLVETSLKGERILGYAEEPCYLWFVMEFCEGG
DLNQYVLSRRPDPATNKSFMLQLTSAIAFLHKNHIVHRDLKPDNILITERSGTPILKVAD
FGLSKVCAGLAPRGKEGNQDNKNVNVNKYWLSSACGSDFYMAPEVWEGHYTAKADIFALG
IIIWAMIERITFIDSETKKELLGTYIKQGTEIVPVGEALLENPKMELHIPQKRRTSMSEG
IKQLLKDMLAANPQDRPDAFELETRMDQVTCAA

SEQ ID NO: 217\_AA498104\_M H29974\_M
PLLLPPPPAAMETGKENGARRGTKSPERKRRSPVQRVLCEKLRPAAQAMDPAGAEVPGEA
FLARRRPDGGGGDVPARPRYSLLAEIGRGSYGVVYEAVAGRSGARVAVKKIRCDAPENVE
LALAEFWALTSLKRRHQNIVQFEECVLQRNGLAQRMSHGNKNSQLYLRLVETSLKGERIL
GYAEEPCYLWFVMEYCEGGDLNQYVLSRRPDPATNKSFMLQLTSAIAFLHKNHIVHRDLK
PDNILITERSGTPILKVADFGLSKVCAGLAPRGKEGNQDNKNVNVNKYWLSSACGSDFYM
APEVWEGHYTAKADIFALGIIIWAMIERITFIDSETKKELLGTYIKQGTEIVPVGEALLE
NPKMELHIPQKRRTSMSEGVKQLLKDMLAANPQDRPDAFELETRMDQVTCAA

SEQ ID NO: 218\_AA215311\_H
MVSSQPKYDLIREVGRGSYGVVYEAVIRKTSARVAVKKIRCHAPENVELALREFWALSSI
KSQHPNVIHLEECILQKDGMVQKMSHGSNSSLYLQLVETSLKGEIAFDPRSAYYLWFVMD
FCDGGDMNEYLLSRKPNRKTNTSFMLQLSSALAFLHKNQIIHRDLKPDNILISQTRLDTS
DLEPTLKVADFGLSKVCSASGQNPEEPVSVNKCFLSTACGTDFYMAPEVWEGHYTAKADI
FALGIIIWAMLERITFIDTETKKELLGSYVKQGTEIVPVGEALLENPKMELLIPVKKKSM
NGRMKQLIKEMLAANPQDRPDAFELELRLVQIAFKDSSWET

SEQ ID NO: 219\_AA018361\_H
MRAAFPAGGAGGSVEPPSARPAPQPAGTAARSEEAPARAQAAGMAGPGWGPPRLDGFILT
ERLGSGTYATVYKAYAKKDTREVVAIKCVAKKSLNKASVENLLTEIEILKGIRHPHIVQL
KDFQWDSDNIYLIMEFCAGGDLSRFIHTRRILPEKVARVFMQQLASALQFLHERNISHLD
LKPQNILLSSLEKPHLKLADFGFAQHMSPWDEKHVLRGSPLYMAPEMVCQRQYDARVDLW
SMGVILYEALFGQPPFASRSFSELEEKIRSNRVIELPLRPLLSRDCRDLLQRLLERDPSR
RISFQDFFAHPWVDLEHMPSGESLGRATALVVQAVKKDQEGDSAAALSLYCKALDFFVPA

#### FIGURE 1X

LHYEVDAQRKEAIKAKVGQYVSRAEELKAIVSSSNQALLRQGTSARDLLREMARDKPRLL AALEVASAAMAKEEAAGGEQDALDLYQHSLGELLLLLRSPRAGGGSCFTLRFRTSWPELN T

SEQ ID NO: 220\_AA311714\_H

MENFILYEEIGRGSKTVVYKGRRKGTINFVAILCTDKCRRPEITNWVRLTREIKHKNIVT
FHEWYETSNHLWLVXENLPEDVVREFGIDLISGLHHLHKLGILFCDISPRKILLEGPGTL
KFSNFCLAKVEGENLEEFFALVAAEEGGGDNGENVLKKSMKSRVKGSPVYTAPEVVRGAD
FSISSDLWSLGCLLYEMFSGKPPFFSESVSELTEKILCEDPLPPIPKDSSRPKASSDFIN
LLDGLLQRDPQKRLTWTRLLQHSFWKKAFAGADQESSVEDLSLSRNTMECSGPQDSKELL
QNSQSRQAKGHKSGQPLGHSFRLENPTEFRPKSTLEGQLNESMFLLSSRPTPRTSTAVEV
SPGEDMTHCSPQKTSPLTKITSGHLSQQDLESQMRELIYTDSDLVVTPIIDNPKIMKQPP
VKFDAKILHLPTYSVDKLLFLKDQDWNDFLQQVCSQIDSTEKSMGASRAKLNLLCYLCVV
AGHQEVATRLLHSPLFQLLIQHLRIAPNWDIRAKVAHVIGLLASHTTELQENTPVVETTS
SIGIGILNCLVQHSTPVPRQCLVYV

SEQ ID NO: 221\_SGK384\_H SLAHVLRARQILTEPEVRDYLRGLVSGLRYLHQRCILHR

SEQ ID NO: 222\_AA210451\_M SGK384\_M MGQQHGTRNGLTHRELPRGVGLLLAMALMNVALYLCLDQLFISPGRSTADSRRCPPGYFR MGRMRNCSRWLSCEELRTEVRQLKRVGEGAVKRVFLSEWKEHKVALSRLTRLEMKEDFLH GLQMLKSLQSEHVVTLVGYCEEDGTILTEYHPLGSLSNLEETLNLSKYQDVNTWQHRLQL AMEYVSIINYLHHSPLGTRVMCDSNDLPKTLSQYLLTSNFSIVANDLDALPLVDHDSGVLIKCGHRELHGDFVAPEQLWPYGEDTPFQDDLMPSYNEKVDIWKIPDVSSFLLGHVEGSDM VRFHLFDIHKACKSQIPAERPTAQNVLDAYQRVFHSLRDTVMSQTKEML

SEQ ID NO: 223\_SGK071\_2\_H
EVVAVQMMVECMDDHYASQALEELMPLLKLRHAHISVYQELFITWNGEISSLYLCLVMEF
NELSFQEVIEDKRKAKKIIDSEWMQNVLGQVLDALEYLHHLDIIHRNLKPSNIILISSDH
CKLQDLSSNVLMTDKAKWNIRAEEDPFRKSWMAPEALNFSFSQKSDIWSLGCIILDMTSC
SFMDGTEAMHLRKSLRQSPGSLKAVLKTMEEKQIPDVETFRNLLPLMLQIDPSDRITIKD
VVHITFLRGSFKSSCVSLTLHRQMVPASITDMLLEGNVASILGDAGDTKGERALKLLSMA
LASYCLVPEGSLFMPLALLHMHDQWLSCDQDRVPGKRDFASLGKLGKLLGPIPKGLPWPP
ELVEVVVTTMELHDRVLDVQLCACSLLLHLLGQALVHHPEAKAPCNQAITSTLLSALQSH
PEEEPLLVMVYSLLAITTTQESESLSEELQNAGLLEHILEHLNSSLESRDVCASGLGLLW
ALLLDDPILALQRPRKKRAPNHGKPGKPKNPASTQSIIVNKAPLEKVPDLISQVLATYPA
DGEMAEASCGVFWLLSLLGCIKEQQFEQVVALLLQSIRLCQDRALLVNNAYRGLASLVKV
SELAAFKVVVQEEGGSGLSLIKETYQLHRDDPEVVENVGMLLVHLASYEEILPELVSSSM
KALLQEIKERFTSSLVSDSSAFSKPGLPPGGSPQLGCTTSGGLE

SEQ ID NO: 224\_AA118352\_M SGK071\_M
EEDPCQKSWMAPEALKFSFSTKSDIWSLGCIILDMATCSFLNDTEAMQLRKAIRHHPGSL
KPILKTMEEKQIPGTDVYYLLLPFMLHINPSDRLAIKDVMQVTFMSNSFKSSSVALNMQR
QKVPIFITDVLLEGNMANILGSWLCASFVNDSRHCDSGIGSQRLGFDFQSVSWTEHPLKD
VMQNFSSRPEVQLRAINKLLTMPEDQLGLPWPTELLEEVISIIKQHGRILDILLSTCSLL
LRVLGQALAKDPEAEIPRSSLIISFLMDTLRSHPNSERLVNVVYNVLAIISSQGQISEEL
EEEGLFQLAQENLEHFQEDRDICLSILSLLWSLLVDVVTVDKEPLEQLSGMVTWVLATHP
EDVEIAEAGCAVLWLLSLLGCIKESQFEQVVVLLLRSIQLCPGRVLLVNNAFRGLASLAK

### FIGURE 1Y

VSELVAFRIVVLEEGSSGLHLIQDIYKLYKDDPEVVENLCMLLAHLTSYKEILPEMESGG IKDLVQVIRGRFTSSLELISYADEILQVLEANAQPGLQEDQLEPPAGQEAPLQGEPLFRP

SEQ ID NO: 225\_018653.9\_H
GRGRGAGHARGLGRGPAGRRAEPPRSLSRPGPGPGSRAGPAGRGEGSDAAPAGGSGRGFL
RLLPAGLRPQRALRSGSEPPRPGQSPEPSPAPGAGRRGGRGELARQIRARYEEVQRYSRG
GPGPGAGRPERRLMDLAPGGPGLPRPRPPWARPLSDGAPGWPPAPGPGSPGPGPRLGCA
ALRNVSGAQYMGSGYTKAVYRVRLPGGAAVALKAVDFSGHDLGSCVREFGVRRGCYRLAA
HKLLKEMVLLERLRHPNVLQLYGYCYQDSEDIPDTLTTITELGAPVEMIQLLQTSWEDRF
RICLSLGRLLHHLAHSPLGSVTLLDFRPRQFVLVDGELKVTDLDDARVEETPCAGSTDCI
LEFPARNFTLPCSAQGWCEGMNEKRNLYNAYRFFFTYLLPHSAPPSLRPLLDSIVNATGE
LAWGVDETLAQLEKVLHLYRSGQYLQNSTASSSTEYQCIPDSTIPQEDYRCWPSYHHGSC
LLSVFNLAEAVDVCESHAQCRAFVVTNQTTWTGRQLVFFKTGWSQVVPDPNKTTYVKASG

SEQ ID NO: 226\_AA396601\_M
TRPGCAALRNVSGAQYVGSGYTKAVYRVRLPGGAAVALKAVDFSGHDLGSCVREFGARRG
CYRLAAHKLLKEMVLLERLRHPNVLQLYGYCYQDSEGIPDTLTTITELGAPVEMIQLLQT
SWEDRFRICLSLGRLLHHLAHSPLGSVTLLDFRPRQFVLVNGELKVTDLDDARVEETPCT
SSADCTLEFPARNFSLPCSAQGWCEGMNEKRNLYNAYRFFFTYLLPHSAPPSLRPLLDSI
VNATGELAWGVDETLAQLETALHLFRSGQYLQNSTSSRAEYQRIPDSAITQEDYRCWPSY
HHGGCLLSVFNLAEAIDVCESHAQCRAFVVTNQTTWTGRKLVFFKTGWNQVVPDAGKTTY
VKAPG

SEQ ID NO: 227\_VRK3\_H
MISFCPDCGKSIQAAFKFCPYCGNSLPVEEHVGSQTFVNPHVSSFQGSKRGLNSSFETSP
KKVKWSSTVTSPRLSLFSDGDSSESEDTLSSSERSKGSGSRPPTPKSSPQKTRKSPQVTR
GSPQKTSCSPQKTRQSPQTLKRSRVTTSLEALPTGTVLTDKSGRQWKLKSFQTRDNQGIL
YEAAPTSTLTCDSGPQKQKFSLKLDAKDGRLFNEQNFFQRAAKPLQVNKWKKLYSTPLLA
IPTCMGFGVHQDKYRFLVLPSLGRSLQSALDVSPKHVLSERSVLQVACRLLDALEFLHEN
EYVHGNVTAENIFVDPEDQSQVTLAGYGFAFRYCPSGKHVAYVEGSRSPHEGDLEFISMD
LHKGCGPSRRSDLQSLGYCMLKWLYGFLPWTNCLPNTEDIMKQKQKFVDKPGPFVGPCGH
WIRPSETLQKYLKVVMALTYEEKPPYAMLRNNLEALLQDLRVSPYDPIGLPMVP

SEQ ID NO: 228\_S71575\_M VRK3\_M
IPTCIGFGIHQDKYRFLVFPSLGRSLQSALDDNPKHVVSERCVLQVACRLLDALEYLHEN
EYVHGNLTAENVFVNPEDLSQVTLVGYGFTYRYCPGGKHVAYKEGSRSPHDGDLEFISMD
LHKGCGPSRRSDLQTLGYCMLKWLYGSLPWTNCLPNTEKITRQKQKYLDSPERLVGLCGR
WNKASETLREYLKVVMALNYEEKPPYATLRNSLEALLQDMRVSPYDPLDLQMVP

SEQ ID NO: 229\_AA45427\_H
MGHALCVCSRGTVIIDNKRYLFIQKLGEGGFSYVDLVEGLHDGHFYALKRILCHEQQDRE
EAQREADMHRLFNHPNILRLVAYCLRERGAKHEAWLLLPFFKRGTLWNEIERLKDKGNFL
TEDQILWLLLGICRGLEAIHAKGYAHRDLKPTNILLGDEGQPVLMDLGSMNQACIHVEGS
RQALTLQDWAAQRCTISYRAPELFSVQSHCVIDERTDVWSLGCVLYAMMFGEGPYDMVFQ
KGDSVALAVQNQLSIPQSPRHSSALRQLLNSMMTVDPHQRPHIPLLLSQLEALQPPAPGQ
HTTQI

SEQ ID NO: 230\_H05721\_H MAVRQALGRGLQLGRALLLRFTGKPGRAYGLGRPGPAAGCVRGERPGWAAGPGAEPRRVG LGLPNRLRFFRQSVAGLAARLQRQFVVRAWGCAGPCGRAVFLAFGLGLIEEKQAESRR

28/113

# FIGURE 1Z

AVSACQEIQAIFTQKSKPGPDPLDTRRLQGFRLEEYLIGQSIGKGCSAAVYEATMPTLPQ NLEVTKSTGLLPGRGPGTSAPGEGQERAPGAPAFPLAIKMMWNISAGSSSEAILNTMSQE LVPASRVALAGEYGAVTYRKSKRGPKQLAPHPNIIRVLRAFTSSVPLLPGALVDYPDVLP SRLHPEGLGHGRTLFLVMKNYPCTLRQYLCVNTPSPRLAAMMLLQLLEGVDHLVQQGIAH RDLKSDNILVELDPDGCPWLVIADFGCCLADESIGLQLPFSSWYVDRGGNGCLMAPEVST ARPGPRAVIDYSKADAWAVGAIAYEIFGLVNPFYGQGKAHLESRSYQEAQLPALPESVPP DVRQLVRALLQREASKRPSARVAANVLHLSLWGEHILALKNLKLDKMVGWLLQQSAATLL ANRLTEKCCVETKMKMLFLANLECETLCQAALLLCSWRAAL

SEQ ID NO: 231\_AI086865\_H

MEKYERIRVVGRGAFGIVHLCLRKADQKLVIIKQIPVEQMTKEERQAAQNECQVLKLLNH

PNVIEYYENFLEDKALMIAMEYAPGGTLAEFIQKRCNSLLEEETILHFFVQILLALHHVH

THLILHRDLKTQNILLDKHRMVVKIGDFGISKILSSKSTPCYISPELCEGKPYNQKSDIW

ALGCVLYELASLKRAFEAANLPALVLKIMSGTFAPISDRYSPELRQLVLSLLSLEPAQRP

PLSHIMAQPLCIRALLNLHTDGREVRGPQQHREQDHQCPLQRGIIMTFGSGSNGCLGHGS

LTDISQPTIVEALLGYEMVQQVEEALSFTLLGSAPLDQEPLLSIDLGTAHSAAVTGEEDL

GSGDVNRLPSWERGHLLAGVASSTDVSTFSEGDCKEPDKCCWRHKQCTGHIIYPFASDCV

RHSLHLHSVNHCNCNSRLKDSSEDSSSSRGAGPTCSHVIESPCFELTPEEEHVERFRYGW

CKSYRPVSVAVIHHPLYHECGADDLNXKKRKRRRKSKPPIPTQVGPATASPDLGTSMAT

GTPDSTAPITIWRSESPTGKGQGSKVIKKVKKKKEKEKDKEEMDEKAKLKKKAKKGQLTK

KKSPVKLEPSPPDVSRSLSARQLARMSESSPESREELESEDSYNGRGQGELSSEDIVESS

SPRKRENTVQAKKTGAKPSQARKVNKRKSPPGSNPNLS

SEQ ID NO: 232\_AA836348\_H

MSVLGEYERHCDSINSDFGSESGGCGDSSPGPSASQGPRAGGGAAEQEELHYIPIRVLGR
GAFGEATLYRRTEDDSLVVWKEVDLTRLSEKERRDALNEIVILALLQHDNIIAYYNHFMD
NTTLLIELEYCNGGNLYDKILRQKDKLFEEEMVVWYLFQIVSAVSCIHKAGILHRDIKTL
NIFLTKANLIKLGDYGLAKKLNSEYSMAETLVGTPYYMSPELCQGVKYNFKSDIWAVGCV
IFELLTLKRTFDATNPLNLCVKIVQGIRAMEVDSSQYSLELIQMVHSCLDQDPEQRPTAD
ELLDRPLLRKRRRSSTVTEAPIAVVTSRTSEVYVWGGGKSTPQKLDVIKSGCSARQVCAG
NTHFAVVTVEKELYTWVNMQGGTKLHGQLGHGDKASYRQPKHVEKLQGKAIRQVSCGDDF
TVCVTDEGQLYAFGSDYYGCMGVDKVAGPEVLEPMQLNFFLSNPVEQVSCGDNHVVVLTR
NKEVYSWGCGEYGRLGLDSEEDYYTPQKVDVPKALIIVAVQCGCDGTFLLTQSGKVLACG
LNEFNKLGLNQCMSGIINHEAYHEVPYTTSFTLAKQLSFYKIRTIAPGKTHTAAIDERGR
LLTFGCNKCGQLGVGNYKKRLGINLLGGPLGGKQVIRVSCGDEFTIAATDEKVLNSKTIR
SNSSGLSIGTVFQSSSPGGGGGGGEEEDSQQESETPDPSGGFRGTMEADRGMEGLISP
TEAMGNSNGASSSCPGWLRKELENAEFIPMPDSPSPLSAAFSESEKDTLPYEELQGLKVA
SEAPLEHKPQVEASVTELFAFESQLVTSAESCSNLCWEGNTTDSSCVCVQLSAGGG

SEQ ID NO: 233\_R86668\_H, MKK6\_H
MNLLLSYRDVQDYSAIIELVETLQALPTCDVAEQHNVCFHYTFALNRRNRPGDRAKALSV
LLPLVQLEGSVAPDLYCMCGRIYKDMFFSSGFQDAGHREQAYHWYRKAFDVEPSLHSGIN
AAVLLIAAGQHFEDSKELRLIGMKLGCLLARKGCVEKMQYYWDVGFYLGAQILANDPTQV
VLAAEQLYKLNAPIWYLVSVMETFLLYQHFRPTPEPPGGPPRRAHFWLHFLLQSCQPFKT
ACAQGDQCLVLVLEMNKVLLPAKLEVRGTDPVSTVTLSLLEPETQDIPSSWTFPVASICG
VSASKRDERCCFLYALPPAQDVQLCFPSVGHCQWFCGLIQAWVTNPDSTAPAEEAEGAGE
MLEFDYEYTETGERLVLGKGTYGVVYAGRDRHTRVRIAIKEIPERDSRFSQPLHEEIALH
RRLRHKNIVRYLGSASQGGYLKIFMEEVPGGSLSSLLRSVWGPLKDNESTISFYTRQILQ
GLGYLHDNHIVHRDIKGDNVLINTFSGLLKISDFGTSKRLAGITPCTETFTGTLQYMAPE
IIDQGPRGYGKAADIWSLGCTVIEMATGRPPFHELGSPQAAMFQVGMYKVHPPMPSSLSA

### FIGURE 1AA

EAQAFLLRTFEPDPRLRASAQTLLGDPFLQPGKRSRSPSSPRHAPRPSDAPSASPTPSAN STTQSQTFPCPQAPSQHPPSPPKRCLSYGGTSQLRVPEEPAAEEPASPEESSGLSLLHQE SKRRAMLAAVLEQELPALAENLHQEQKQEQGARLGRNHVEELLRCLGAHIHTPNRRQLAQ ELRALQGRLRAQGLGPALLHRPLFAFPDAVKQILRKRQIRPHWMFVLDSLLSRAVRAALG VLGPEVEKEAVSPRSEELSNEGDSQQSPGQQSPLPVEPEQGPAPLMVQLSLLRAETDRLR EILAGKEREYQALVQRALQRLNEEARTYVLAPEPPTALSTDQGLVQWLQELNVDSGTIQM LLNHSFTLHTLLTYATRDDLIYTRIRGGMVCRIWRAILAQRAGSTPVTSGP

SEQ ID NO: 234\_PAK6\_H

MFGKKKKKIEISGPSNFEHRVHTGFDPQEQKFTGLPQQWHSLLADTANRPKPMVDPSCIT

PIQLAPMKTIVRGNKPCKETSINGLLEDFDNISVTRSNSLRKESPPTPDQGASSHGPGHA

EENGFITFSQYSSESDTTADYTTEKYREKSLYGDDLDPYYRGSHAAKQNGHVMKMKHGEA

YYSEVKPLKSDFARFSADYHSHLDSLSKPSEYSDLKWEYQRASSSSPLDYSFQFTPSRTA

GTSGCSKESLAYSESEWGPSLDDYDRRPKSSYLNQTSPQPTMRQRSRSGSGLQEPMMPFG
ASAFKTHPQGHSYNSYTYPRLSEPTMCIPKVDYDRAQMVLSPPLSGSDTYPRGPAKLPQS
QSKSGYSSSSHQYPSGYHKATLYHHPSLQSSSQYISTASYLSSLSLSSSTYPPPSWGSSS
DQQPSRVSHEQFRAALQLVVSPGDPREYLANFIKIGEGSTGIVCIATEKHTGKQVAVKKM
DLRKQQRRELLFNEVVIMRDYHHDNVVDMYSSYLVGDELWVVMEFLEGGALTDIVTHTRM
NEEQIATVCLSVLRALSYLHNQGVIHRDIKSDSILLTSDGRIKLSDFGFCAQVSKEVPKR
KSLVGTPYWMAPEVISRLPYGTEVDIWSLGIMVIEMIDGEPPYFNEPPLQAMRRIRDSLP
PRVKDLHKVSSVLRGFLDLMLVREPSQRATAQELLGHPFLKLAGPPSCIVPLMRQYRHH

SEQ ID NO: 235\_SURTK106\_H
MNDRNEIQMEAKLQSLTIIAQEILCRFFITLRRHARFLLTKLGRQGMARSGITHSCAVCI
LCGPSREGDSPVAMGMTRMLLECSLSDKLCVIQEKQYEVIIVPTLLVTIFLILLGVILWL
FIREQRTQQQRSGPQGIAPVPPPRDLSWEAGHGGNVALPLKETSVENFLGATTPALAKLQ
VPREQLSEVLEQICSGSCGPIFRANMNTGDPSKPKSVILKALKEPAGLHEVQDFLGRIQF
HQYLGKHKNLVQLEGCCTEKLPLYMVLEDVAQGDLLGFLWTCRRDVMTMDGLLYDLTEKQ
VYHIGKQVLLALEFLQEKHLFHGDVAARNILMQSDLTAKLCGLGLAYEVYTRGAISSTQT
IPLKWLAPERLLLRPASIRADVWSFGILLYEMVTLGAPPYPEVPPTSILEHLQRRKIMKR
PSSCTHTMYSIMKSCWRWREADRPSPRELRLRLEAAIKTADDEAVLQVPELVVPELYAAV
AGIRVESLFYNYSML

SEQ ID NO: 236\_AA098024\_M LQEKHLFHGDVAARNILIQSDLTPKLCHLGLAYEVHAHGAISSARSSTIPLKWLAPERLL LRPASIRGDIWSFGILLYEMVTLGAPPYPEVPPTSILQYLQRKKIMKRPSSCSHAMYNIM KCCWRWSEDSRPLLVQLLQRLEAASRSADDKAVLQVPELVVPELYADVAGIRAESISYSF SVL

SEQ ID NO: 237\_SGK2ALPHA\_H
MNSSPAGTPSPQPSRANGNINLGPSANPNAQPTDFDFLKVIGKGNYGKVLLAKRKSDGAF
YAVKVLQKKSILKKKEQSHIMAERSVLLKNVRHPFLVGLRYSFQTPEKLYFVLDYVNGGE
LFFHLQRERRFLEPRARFYAAEVASAIGYLHSLNIIYRDLKPENILLDCQGHVVLTDFGL
CKEGVEPEDTTSTFCGTPEYLAPEVLRKEPYDRAVDWWCLGAVLYEMLHGLPPFYSQDVS
QMYENILHQPLQIPGGRTVAACDLLQSLLHKDQRQRLGSKADFLEIKNHVFFSPINWDDL
YHKRLTPPFNPNVTGPADLKHFDPEFTQEAVSKSIGCTPDTVASSSGASSAFLGFSYAPE
DDDILDC

# FIGURE 1BB

SEQ ID NO: 238\_CCRK\_H
MDQYCILGRIGEGAHGIVFKAKHVETGEIIALKKVALRRLEDGFPNQALREIKALQEMED
NQYVVQLKAVFPHGGGFVLAFEFMLSDLAEVVRHAQRPLAQAQVKSYLQMLLKGVAFCHA
NNIVHRDLKPANLLISASGQLKIADFGLARVFSPDGSRLYTHQVATRSVGCIMGELLNGS
PLFPGKNDIEQLCYVLRILGTPNPQVWPELTELPDYNKISFKEQVPMPLEEVLPDVSPQA
LDLLGQFLLYPPHQRIAASKALLHQYFFTAPLPAHPSELPIPQRLGGPAPKAHPGPPHIH
DFHVDRPLEGVAVEPRADSALHPGGVRSWPWSRLPAPQDHSVHLFLCHLPGFTLQGLPMA
TVGPHHTLPLSPCEGWSRGRGHVPSQEYENIQSSRGDSWPVLGEPYLLCATDVPIRTVSS
AASQGLHMQNDDACLGAASPECCLLVKEKCRE

SEQ ID NO: 239\_TESK2\_H
MDRSKRNSIAGFPRVERLEEFEGGGGGEGNVSQVGRVWPSSYRALISAFSRLTRLDDFT
CEKIGSGFFSEVFKVRHRASGQVMALKMNTLSSNRANMLKEVQLMNRLSHPNILRYINSG
NLEQLLDSNLHLPWTVRVKLAYDIAVGLSYLHFKGIFHRDLTSKNCLIKRDENGYSAVVA
DFGLAEKIPDVSMGSEKLAVVGSPFWMAPEVLRDEPYNEKADVFSYGIILCEIIARIQAD
PDYLPRTENFGLDYDAFQHMVGDCPPDFLQLTFNCCNMDPKLRPSFVEIGKTLEEILSRL
QEEEQERDRKLQPTARGLLEKAPGVKRLSSLDDKIPHKSPCPRRTIWLSRSQSDIFSRKP
PRTVSVLDPYYRPRDGAARTPKVNPFSARQDLMGGKIKFFDLPSKSVISLVFDLDAPGPG
TMPLADWQEPLAPPIRRWRSLPGSPEFLHQEACPFVGREESLSDGPPPRLSSLKYRVKEI
PPFRASALPAAQAHEAMDCSILQEENGFGSRPQGTSPCPAGASEEMEVEERPAGSTPATF
STSGIGLQTQGKQDG

### FIGURE 2A

SEQ ID NO: 1 X69117 H BARK2 H AAGGCGACCCCGGCCCCGCCCAGCAAGAGGATCGTCCTGCCGGAGCCCAGTATCCGG AGTGTGATGCAGAAGTACCTTGCAGAGAGAAATGAAATAACCTTTGACAAGATTTTCAAT CCTCAGGTGAAGTTTTATGAAGAGATAAAGGAATATGAAAAACTTGATAATGAGGAAGAC CGCCTTTGCAGAAGTCGACAAATTTATGATGCCTACATCATGAAGGAACTTCTTTCCTGT TCACATCCTTTCTCAAAGCAAGCTGTAGAACACGTACAAAGTCATTTATCCAAGAAACAA GTGACATCAACTCTTTTTCAGCCATACATAGAAGAAATTTGTGAAAGCCTTCGAGGTGAC ATTTTTCAAAAATTTATGGAAAGTGACAAGTTCACTAGATTTTGTCAGTGGAAAAACGTT GAATTAAATATCCATTTGACCATGAATGAGTTCAGTGTGCATAGGATTATTGGACGAGGA GGATTCGGGGAAGTTTATGGTTGCAGGAAAGCAGACACTGGAAAAATGTATGCAATGAAA TGCTTAGATAAGAAGAGGATCAAAATGAAACAAGGAGAAACATTAGCTTTAAATGAAAGA TTCCATACCCCAGATAAACTCTGCTTCATCCTGGATCTGATGAACGGGGGGCGATTTGCAC TACCACCTTTCACAACACGGTGTGTTCTCTGAGAAGGAGATGCGGTTTTATGCCACTGAA ATCATTCTGGGTCTGGAACACGTGCACAATCGGTTTGTTGTCTACAGAGATTTGAAGCCA GCAAATATTCTCTTGGATGAACATGGACACGCAAGAATATCAGATCTTGGTCTTGCCTGC GATTTTTCCAAAAAGAAGCCTCATGCGAGTGTTGGCACCCATGGGTACATGGCTCCCGAG GTGCTGCAGAAGGGGACGGCCTATGACAGCAGTGCCGACTGGTTCTCCCTGGGCTGCATG CTTTTCAAACTTCTGAGAGGTCACAGCCCTTTCAGACAACATAAAACCAAAGACAAGCAT GAAATTGACCGAATGACACTCACCGTGAATGTGGAACTTCCAGACACCTTCTCTCCTGAA CTGAAGTCCCTTTTGGAGGGCTTGCTTCAGCGAGACGTTAGCAAGCGGCTGGGCTGTCAC GGAGGCGGCTCACAGGAAGTAAAAGAGCACAGCTTTTTCAAAGGTGTTGACTGGCAGCAT GTCTACTTACAAAAGTACCCACCACCCTTGATTCCTCCCCGGGGAGAAGTCAATGCTGCT GATGCCTTTGATATTGGCTCATTTGATGAAGAGGATACCAAAGGGATTAAGCTACTTGAT TGCGACCAAGAACTCTACAAGAACTTCCCTTTGGTCATCTCTGAACGCTGGCAGCAAGAA GTAACGGAAACAGTTTATGAAGCAGTAAATGCAGACACAGATAAAATCGAGGCCAGGAAG AGAGCTAAAAATAAGCAACTTGGCCACGAAGAAGATTACGCTCTGGGGAAGGACTGTATT ATGCACGGGTACATGCTGAAACTGGGAAACCCATTTCTGACTCAGTGGCAGCGTCGCTAT CTGACAATGGAACAGATTCTCTCTGTGGAAGAAACTCAAATTAAAGACAAAAAATGCATT TTGTTCAGAATAAAAGGAGGGAAACAATTTGTCTTGCAATGTGAGAGTGATCCAGAGTTT GTGCAGTGGAAGAAGAGTTGAACGAAACCTTCAAGGAGGCCCAGCGGCTATTGCGTCGT GCCCGAAGTTCCTCAACAAACCTCGGTCAGGTACTGTGGAGCTCCCAAAGCCATCCCTC TGTCACAGGAACAGCAACGGCCTCTGA

# FIGURE 2B

SEO ID NO: 3 AA826850 H GAAGAGGATGGGCTCCATGTCGGCGGCGCCGCGGGGGGCCGGTGTTTGACGACAA GGAGGACGTGAACTTCGACCACTTCCAGATCCTTCGGGCCATTGGGAAGGGCAGCTTTGG CAAGGTGTGCATTGTGCAGAAGCGGGACACGGAGAAGATGTACGCCATGAAGTACATGAA CAAGCAGCAGTGCATCGAGCGCGACGAGGTCCGCAACGTCTTCCGGGAGCTGGAGATCCT GCAGGAGATCGAGCACGTCTTCCTGGTGAACCTCTGGTACTCCTTCCAGGACGAGGAGGA CATGTTCATGGTCGTGGACCTGCTACTGGGCGGGGACCTGCGCTACCACCTGCAGCAGAA CGTGCAGTTCTCCGAGGACACGGTGAGGCTGTACATCTGCGAGATGGCACTGGCTCTGGA CTACCTGCGCGGCCAGCACATCATCCACAGAGATGTCAAGCCTGACAACATTCTCCTGGA TGAGAGAGACATGCACACCTGACCGACTTCAACATTGCCACCATCATCAAGGACGGGGA GCGGGCGACGCATTAGCAGCCACCAAGCCGTACATGGCTCCGGAGATCTTCCAXTCTTT TGTCAACGGCGGACCGGCTACTCCTTCGAGGTGGACTGGTGGTCGGTGGGGGTGATGGC CTATGAGCTGCTGCGAGGATGGAGGCCCTATGACATCCACTCCAGCAACGCCGTGGAGTC CCTGGTGCAGCTGTTCAGCACCGTGAGCGTCCAGTATGTCCCCACGTGGTCCAAGGAGAT GGTGGCCTTGCTGCGGAAGCTCCTCACTGTGAACCCCGAGCACCGGCTCTCCAGCCTCCA GGACGTGCAGCAGCCCCGGCGCTGCCGGCGTGCTGTGGGACCACCTGAGCGAGAAGAG GGTGGAGCCGGGCTTCGTGCCCAACAAAGGCCGTCTGCACTGCGACCCCACCTTTGAGCT GGAGGAGATGATCCTGGAGTCCAGGCCCCTGCACAAGAAGAAGAAGCGCCTGGCCAAGAA CAAGTCCCGGGACAACAGCAGGGACAGCTCCCAGTCCGAGAATGACTATCTTCAAGACTG CCTCGATGCCATCCAGCAAGACTTCGTGATTTTTAACAGAGAAAAGCTGAAGAGGAGCCA GGACCTCCCGAGGGAGCCTCTCCCCGCCCCTGAGTCCAGGGATGCTGCGGAGCCTGTGGA GGACGAGGCGGAACGCTCCGCCCTGCCCATGTGCGGCCCCATTTGCCCCTCGGCCGGGAG CGGCTAGGCCGGGATGCCCGTGGTCCTCACCCCTTGAGCTGCTTTGGAGACTCGGCTGCC GCCCACAGTGCCCCGGACACATTTCACACCTCAGGCTCGTGGTGCTGCAGGGGACAAGAG GCTGTGGGTGCAGGGGACACCTGTGGAGGGCATTTCCCGTGGGCCCCCGAGACCCGCCTA GATGGAGGAAGCGCTGCTGGGCGCCCTCTTACCGCTCACGGGGAGCTGGGGCCATGGATG GGACAGGAGTCTTTGTCCCTGCTCAGCCCGGAGGCTGTGCACGGCCCTCGTCACAAGGTG ACCCTTGCAGCACAGGCCGCGGGTGCCCCAGGCTCGGCTCAGTTCTTGGAGGTCAAGGGC ATGGGTTGGGGTGGGGGGGGGGGTGAATGTTTTCTAGAGATTCAAACTGCTCCAGCA ATTTCTGTATAGTTTTCACCTCTGAGAATTACAATGTGAGAACCGCTC

SEQ ID NO: 4\_AA960957\_H
GTCCCACATCCGGCATCCGGCATCCCAGCGGCCGGCCATGTAGCAGCGGCAGCAACGGCG
GAATATGGGCGGGAACCACTCCCACAAGCCCCCCGTGTTTGACGAGAATGAGGAAGTCAA
CTTTGACCATTTTCAGATTCTGCGGGCCATTGGTAAAGGGAGTTTTGGAAAGGTATGCAT
CGTGCAGAAGCGAGACACTAAGAAAATGTATGCAATGAAGTACATGAACAAGCAGAAGTG
CATCGAGAGGGGATGAGGTTCGGAATGTTTTCCGGGAGCTGCAGATCATGCAAGGGCTGGA

#### FIGURE 2D

SEQ ID NO: 5 TBK1 H GTATAACAAGAGGATTGCCTGATCCAGCCAAGATGCAGAGCACTTCTAATCATCTGTGGC TTTTATCTGATATTTTAGGCCAAGGAGCTACTGCAAATGTCTTTCGTGGAAGACATAAGA ATGTTCAAATGAGAGAATTTGAAGTGTTGAAAAAACTCAATCACAAAAATATTGTCAAAT TATTTGCTATTGAAGAGAGACAACAACAAGACATAAAGTACTTATTATGGAATTTTGTC CATGTGGGAGTTTATACACTGTTTTAGAAGAACCTTCTAATGCCTATGGACTACCAGAAT GTATAGTGCACCGTGATATCAAGCCAGGAAATATCATGCGTGTTATAGGGGAAGATGGAC AGTCTGTGTACAAACTCACAGATTTTGGTGCAGCTAGAGAATTAGAAGATGATGAGCAGT TAAGAAAAGATCATCAGAAGAAATATGGAGCAACAGTTGATCTTTGGAGCATTGGGGTAA CATTTTACCATGCAGCTACTGGATCACTGCCATTTAGACCCTTTGAAGGGCCTCGTAGGA ATAAAGAAGTGATGTATAAAATAATTACAGGAAAGCCTTCTGGTGCAATATCTGGAGTAC AGAAAGCAGAAAATGGACCAATTGACTGGAGTGGAGACATGCCTGTTTCTTGCAGTCTTT CTCGGGGTCTTCAGGTTCTACTTACCCCTGTTCTTGCAAACATCCTTGAAGCAGATCAGG AAAAGTGTTGGGGTTTTGACCAGTTTTTTGCAGAAACTAGTGATATACTTCACCGAATGG TAATTCATGTTTTTTCGCTACAACAAATGACAGCTCATAAGATTTATATTCATAGCTATA AAGAACTTATCTACGAAGGGCGACGCTTAGTCTTAGAACCTGGAAGGCTGGCACAACATT TCCCTAAAACTACTGAGGAAAACCCTATATTTGTAGTAAGCCGGGAACCTCTGAATACCA TAGGATTAATATATGAAAAATTTCCCTCCCTAAAGTACATCCACGTTATGATTTAGACG GGGATGCTAGCATGGCTAAGGCAATAACAGGGGTTGTGTGTTATGCCTGCAGAATTGCCA GTACCTTACTGCTTTATCAGGAATTAATGCGAAAGGGGATACGATGGCTGATTGAATTAA TTAAAGATGATTACAATGAAACTGTTCACAAAAAGACAGAAGTTGTGATCACATTGGATT TCTGTATCAGAAACATTGAAAAAACTGTGAAAGTATATGAAAAGTTGATGAAGATCAACC TGGAAGCGGCAGAGTTAGGTGAAATTTCAGACATACACACCAAATTGTTGAGACTTTCCA GTTCTCAGGGAACAATAGAAACCAGTCTTCAGGATATCGACAGCAGATTATCTCCAGGTG GATCACTGGCAGACGCATGGGCACATCAAGAAGGCACTCATCCGAAAGACAGAAATGTAG AAAAACTACAAGTCCTGTTAAATTGCATGACAGAGATTTACTATCAGTTCAAAAAAAGACA AAGCAGAACGTAGATTAGCTTATAATGAAGAACAAATCCACAAATTTGATAAGCAAAAAC TGTATTACCATGCCACAAAAGCTATGACGCACTTTACAGATGAATGTGTTAAAAAAGTATG AGGCATTTTTGAATAAGTCAGAAGAATGGATAAGAAAGATGCTTCATCTTAGGAAACAGT TATTATCGCTGACTAATCAGTGTTTTGATATTGAAGAAGAAGTATCAAAATATCAAGAAT ATACTAATGAGTTACAAGAAACTCTGCCTCAGAAAATGTTTACAGCTTCCAGTGGAATCA AACATACCATGACCCCAATTTATCCAAGTTCTAACACATTAGTAGAAATGACTCTTGGTA TGAAGAAATTAAAGGAAGAGATGGAAGGGGTGGTTAAAGAACTTGCTGAAAATAACCACA TTTTAGAAAGGTTTGGCTCTTTAACCATGGATGGTGGCCTTCGCAACGTTGACTGTCTTT AGCTTTCTAATAGAAGTTTAAGAAAAGTTTCCGTTTGCACAAGAAAATAACGCTTGGGCA TTAAATGAATGCCTTTATAGATAGTCACTTGTTTCTACAATCCAGTATTTGATGTGGTCG TGTAAATATGTACAATATTGTAAATACATAAAAAATATACAAATTTTTTGGCTGCTGTGAA GATGTAATTTTATCTTTTAACATTTATAATTATATGAGGAAATTTGACCTCAGTGATCAC GAGAAGAAAGCCATGACCGACCAATATGTTGACATACTGATCCTCTACTCTGAGTGGGGC TAAATAAGTTATTTTCTCTGACCGCCTACTGGAAATATTTTTAAGTGGAACCAAAATAGG CATCCTTACAAATCAGGAAGACTGACTTGACACGTTTGTAAATGGTAGAACGGTGGCTAC TGTGAGTGGGGAGCAGAACCGCACCACTGTTATACTGGGATAACAATTTTTTTGAGAAGG ATAAAGTGGCATTATTTTATTTTACAAGGTGCCCAGATCCCAGTTATCCTTGTATCCATG TAATTTCAGATGAATTATTAAGCAAACATTTTAAAGTGAATTCATTATTAAAAACTATTC ATTTTTTCCTTTGGCCATAAATGTGTAATTGTCATTAAAATTCTAAGGTCATTTCAACT

### FIGURE 2C

GCACCCCTTCCTGGTCAATCTGTGGTACTCCTTCCAGGATGAGGAGGACATGTTCATGGT GGTGGACCTGCTCCTGGGAGGCGACCTGCGCTACCATCTGCAGCAGAATGTGCATTTCAC AGAGGGGACTGTGAAACTCTACATCTGTGAGCTGGCACTGGCCCTGGAGTATCTTCAGAG GTACCACATCATCCACAGAGACATCAAGCCAGACAATATCCTGCTGGATGAACACGGACA TGTTCACATTACAGACTTCAACATAGCGACGGTAGTGAAAGGAGCAGAAAGGGCTTCCTC CATGGCTGGCACCAAGCCCTACATGGCTCCAGAAGTATTCCAGGTGTACATGGACAGAGG CCCCGGATACTCGTACCCTGTCGACTGGTGGTCCCTGGGCATCACAGCCTATGAGCTGCT GCGGGGCTGGAGGCCGTACGAAATCCACTCGGTCACGCCCATCGATGAAATCCTCAACAT GTTCAAGGTGGAGCGTGTCCACTACTCCTCCACGTGGTGCAAGGGGATGGTGGCCCTGCT GAGGAAGCTCCTGACCAAGGATCCTGAGAGCCGCGTGTCCAGCCTTCATGACATACAGAG CGTGCCCTACTTGGCCGACATGAACTGGGACGCGGTGTTCAAGAAGGCACTGATGCCCGG CTTTGTGCCCAATAAAGGGAGGTTGAACTGCGATCCCACATTTGAGCTTGAAGAGATGAT TCTAGAATCCAAGCCACTTCACAAAAAGAAGAAGCGATTGGCAAAGAACAGATCCAGGGA TGGCACAAAGGACAGCTGCCCGCTGAATGGACACCTGCAGCACTGTTTGGAGACTGTCCG GGAGGAATTCATCATATTCAACAGAGAGAGCTCAGGAGGCAGCAGGGACAGGGCAGCCA CAACAACAACCTCCTCACCCACACCTGCACCCGTGGCTGCAGCAGCTGAGCCCACACTTG CCTGATGGTCCCTGTCTCACCCCTGAAAACATCAGATGCAGAAAAAGCCCTGGACTTGGA GCTGGGAAGCCTGGGTTCTGGTCCCATCTCCATGACTGATTCACGTGTGACCTCAGACAA GTCACGCCCTCTCTGTGCCTCCGTTTTCTGCATCTGCCAAAGGGGGTTAAACACTTCTGCC TGATATTTATAAAATCATTTTTACGTGCAAAATATAACCTTAATATTTGAAGTGACCCCC ATTCCCCAAAGCAATCAAACCGTCATGACTTTGCAATTTGGCACATCCTAGCTTGTTAGA GGGCACTTCCGAAAAACACAGCCCTGACAGCAAAATAAAGGTCTGATATGTTGGCCCCTT CTATGGAAACAACGCTGCCAAATCCTGGAGCAAAACCTGAAGTGTCTTCATGTGCATTCT CTGGCAGGCCACAGTCCTGAGCTTGTAAGATGGTGCAGCATGCAGACCAGACTTGTCCCC AAGGTCTCAGCGCTGCGGTCTCACTCCTCCCCTCATTTAAGAAGACTATCCTTACCTTTT AGTTTCAGCAGTCCTCACCACCACCATATCCCCAGTGCTGGGATGGCACACAGGTGTCCA TTCAGATGAGAGTTGGGTCGCTGAGCATTGGTTACTCCTGCAGAGTGTAATCAGCACCCC ATCCAACTGGCCCGAAAGCCCAGACCTGCAGCAGAACTCTCCAACTCTCTATCAGCTTTC AGGGTTTTCTCTCCTGGGAAGGGTGTAAAATCAGCTTGTCAGATTCTTCTTACAGAGAGT ATCCAATCGGTATTGGTGGAGCGGCTCCCTATTTATACAATAGGAAGCATGGGTGCTTAG AAAGTTTATTTCAGGAGGAAAATGGGTTCACACAAAAAGCAAACTACATTCTGATCTGCT CAGGGAGAAGCTTGCCTTTGAACTGGAAGATGTTGGGATGAGCAGGGAAAGCTTAGACTT AGGCAAAGCATGCAATCGCTCTGAATGGCAGTTTCCTCATTTTTAAACAGGGATAATAAA ACTAATATTGCAGGGGAGTTACAGGGTTAAATAAGATCCTGTGTGTAACCCCAAGCATTG GATGACTCATAGAATGGCCTTTTTTGTCAGCATAATCGTCATCATTATTTAGATACTTTC AAATGTTCTTCCTGGGGTCTTTGATATTTGTTTGTTACATCCTGCTGAAGTTCGACTGTG TTTTTATTTTTCATCCAACTTCCATTTTTCACTTTTTACATGATTACTCAATCCTTGGG GCTGTCCATGTCATCTCTTAGATTTCTTAAAAGACATTTTAATGTATGGTTAGGTTTTAT ATTTTTTTTTTTTAAAAAAGAAATAGTCAGTGTTTTCCTCCTTTCAACCGAGACTATTTC TGGATTGTGTGCTCCTCGTCAGTTGACTTGTTTTGCACACTTTTCTTTACTTCATGTCCC CATCAACAACCGTCCTGCTCCCCACCTCCCCCAGGAAATAAGGGGCCTGCTCCTCTCCCT ATTAGGGGCAGGAGCTGGAAGTCGCCCTAGGAACACCAGATTTCCTGGTTCTGTTCAAGT TGGCATTTCTTGTTTGGAATAAACTATTTCTTGGACATTCCTTC

#### FIGURE 2E

SEQ ID NO: 6 AA305176\_H TGGCTGCTCGCGGAGGGCAGTGTACGCGGGGCCGCTGTAGGCTGTCCAGCGATGGATCC CACCGCGGGAAGCAAGAAGGAGCCTGGAGGAGGCGCGCGACTGAGGAGGGCGTGAATAG GATCGCAGTGCCAAAACCGCCCTCCATTGAGGAATTCAGCATAGTGAAGCCCATTAGCCG GGGCGCCTTCGGGAAAGTGTATCTGGGGCAGAAAGGCGGCAAATTGTATGCAGTAAAGGT TGCACTGGCACTAAGCAAAAGCCCATTCATTGTCCATTTGTATTATTCACTGCAGTCTGC AAACAATGTCTACTTGGTAATGGAATATCTTATTGGGGGAGATGTCAAGTCTCCTACA TATATATGGTTATTTTGATGAAGAGATGGCTGTGAAATATATTTCTGAAGTAGCACTGGC TCTAGACTACCTTCACAGACATGGAATCATCCACAGGGACTTGAAACCGGACAATATGCT TATTTCTAATGAGGGTCATATTAAACTGACGGATTTTGGCCTTTCAAAAGTTACTTTGAA TAGAGATATTAATATGATGGATATCCTTACAACACCATCAATGGCAAAACCTAGACAAGA TTATTCAAGAACCCCAGGACAAGTGTTATCGCTTATCAGCTCGTTGGGATTTAACACACC ACAGCTTTCTCAAGGACTCGTATGCCCTATGTCTGTAGATCAAAAGGACACTACGCCTTA TTCTAGCAAATTACTAAAATCATGTCTTGAAACAGTTGCCTCCAACCCAGGAATGCCTGT GAAGTGTCTAACTTCTAATTTACTCCAGTCTAGGAAAAGGCTGGCCACATCCAGTGCCAG TAGTCAATCCCACACCTTCATATCCAGTGTGGAATCAGAATGCCACAGCAGTCCCAAATG AATGAATGTGAGAAATATTATACCTTTTCATATAAATTCCATAAAGAAATGAAATTGTTA CATGAATGGCAGTCATAGTATTAATCAGAAATTCATTTTCCTGCACATTCTGTCAAATTC TTTTGAAATATTTCATTTCTCATTCAATTGTGACATTGTTCTTACTTGATTATAAATGA GATTCTTGCAGTAAATTGATAATAAATGCTTGGCTTCTGTGTATCTAGGTGGACCTCACT TGTTTTTAGAAGTCCTTCCCATGATACAGACATTGGCTTGTTGGTTTTGTTTTATTTTGT TTTTAACATATGTCATTTAAAAACTCATATTACCTCCTTTT

SEQ ID NO: 7\_AA116841\_M
CCACGCGTCCGATCCCATGGCCAGAAGGCGAAGAAAAGCTATCTGATAATGCTCAAAGTG
CAATGGACATGCTTTTAACCATTGATGATTCAAAGAGAGCTGGAATGAGAGAACTAAAAC
AGCATCCTCTCTCAGTGAAGTGGACTGGGAAAATCTGCAGCATCAGACTATGCCTTTCG
TACCCCAACCAGACGACGAAACAGATACATCCTATTTTGAAGCCAGAAATAATGCTCAAC
ATCTGACCGTATCTGGGTTTAGTCTGTAGCACATGCGTGTCATTTTTATCTAACTTGTGA
TATAGAATTAAGTTTTACAGTAATATGCTACTTAATACTAGATTGGTCTAAATGGGATAA
AAGTCATTATTTTACCCAGACTGAACAGCTTTTAATTACTAAGTACAACAGTTTTTACAG
AATTAAAATACTATAAGCAATATAATCAGTAATTAATCTTTACCTTAGAACTGTATATAA
GCCATAATAGCTTTTTCATCTTATTTATTCACTGCACTTTATGAAGAGCAAAGTATCAA
TAAACTAAAACACTACCACTCTAAATAGAGGGGAGTGAGCCGT

#### FIGURE 2F

GGCCCATATCCGAGCAGAAGAGATATTTTGGTAGAAGCAGATGGTGCCTGGGTGGTGAA GATGTTTTACAGTTTTCAGGATAAGAGGAATCTTTATCTAATCATGGAATTTCTCCCTGG AGGTGACATGACATTGCTAATGAAGAAAGACACCTTGACAGAAGAGGAAACACAGTT GGATATTAAGCCAGACAACCTTTTATTGGATGCCAAGGGTCATGTAAAATTATCTGATTT TGGTTTATGTACGGGATTAAAGAAAGCTCACAGGACTGAATTTTATAGAAATCTCACACA CAACCCACCAAGTGACTTCTCATTTCAGAACATGAACTCAAAGAGGAAAGCAGAAACTTG GAAGAAGAACAGGAGACAACTGGCATATTCCACAGTTGGGACACCAGATTACATTGCTCC AGAAGTATTCATGCAGACTGGTTACAACAAATTGTGTGACTGGTGGTCTTTGGGAGTGAT TATGTATGAAATGCTAATAGGATATCCACCTTTCTGCTCTGAAACACCTCAAGAAACATA CAGAAAAGTGATGAACTGGAAAGAAACTCTGGTATTTCCTCCAGAGGTACCTATATCTGA GAAAGCCAAGGACTTAATTCTCAGATTTTGTATTGATTCTGAAAACAGAATTGGAAATAG TGGAGTAGAAGAATAAAAGGTCATCCCTTTTTTGAAGGTGTCGACTGGGAGCACATAAG GGAAAGGCCAGCAGCAATCCCTATAGAAATCAAAAGCATTGATGATACTTCAAATTTTGA TGACTTCCCTGAATCTGATATTTTACAACCAGTGCCAAATACCACAGAACCGGACTACAA ATCCAAAGACTGGGTTTTTCTCAATTATACCTATAAAAGGTTTGAAGGGTTGACTCAACG TGAAATACTCCTGAAGATGGTGGTGCTTATTGACTACAAGAGGAAATTCTACAGGATTAG GATTTCTAAGACTACTATAGGAATTGGTTGGCAGTGCCAGCTGGCTCTTTTTTTAATAT TTTATTATTTTTGTTAACTTTATTATGAAGGTACTGGAATAAAAGGAACAGACATCCC TTGAACTGTAACACCTCTAATCAATTCAGGAGAAACACATATCATTTAAAGCAACATAGG CTAACCTGTAGGTAACACTGCAGTATTGATGTTTTACTGCAAATCTTATGGGTCTAGATA ATCAGTAAAAGCCATCTTCCATAGTTGGTGTTAGAACATTGCCCTATTGGTTTGGACATC TGTAGAATATATGAAGACAATTTCTGTAATGGTTTTAAGAGATTTAAAAAGAAATTCA CTGGTTCTTTACAAAATAGAATTTATCATCAAGTTATTACACAAACTTCACAGTAAGGAG TGACAAGTTTATAATAAGGAAGACAAAGTTTAACACCTTCACTCAAGCACTCCACTAATA TATTTACGTTGCATTCAGAAATACTGATGACCTTCATATACGTAGTCTGTATACTCATAG GGAGATGTACTGTATTATATAACATGTAAAGTTGATTTTCTTGTGACAAGAGAACTTCTT TTTTTAACAAGAGGACATGGCATTATTTTAATTTGATTATGGTGAGTTGAATTTAAGACA TGACCATGAAGGCTGCTTGTAGAATTAGTGTATTTTTATTAAACTATTTTTTAAATGTC AAACTTCTATCATGTAAATGGACTTATAGAGAACAAAAAGCTATTTACTTTGGTTTTCTA GAAAGTTGTTACATATCATGGCTGGTTAACTTTTATTTCTTTTGATGAAAATTTTTCCTT TGATAGTACTTGTATTATTGTGCCATTATTTTCTTATGCTCCAAATGTACCAAAGATCTT GAACAGAGTGGATGTTCACAACTGAGTAGAATTTTCCTTTCCTGTGGGCATGCTGTATTC AGACCTGACAGATCTTTGATAGAGGTCAGCTTATTAAAGGGCCAATATTGTTCTTGTTTAG CTACATCACTGTGGTGAATATAGATGGAATTAAGGAAGTAAATGCAGGCCAGGGGGTTGT GATGAGAGGATAGGGGAGATAATATCAGCATCAAATTCTTTGGGTATCTCTCTAAGAATT AAATAATCTTTTCTAGCTTAATATTTTAATTCTAATTCAAACAACTCTGAGGTTTTGGTT TCATTAGTAATAGTTGAGGAATAATATACTAGCAAAGAATGGCCTAATGTTTGTCATAAC TGTTAATGGATGAAATTTTTTAAAGATACAACCATGATAACCATTATAAATGATCTATGA TCAAAATCTAAAGTGATGAATTATTTGTAGGAATGTCTTCCTAATGGGGAAGAATTGCAT AGGAGCATTATGCAAATCTACACAAGCTTTTATAAATGTTGCTGCTGGGTAGCTCCACAG ATATTTGTTGAGTACTTACGTGTTTATCTAACAGTTCACTTCCATTTTTCTAGTCTGGAT TTTTTGAGTATTTAGGAAAGAGAGCTATTAAAAACTCTGGGGATTTCTCAATGTGACTAA CTCTAATTTTCTAATTATAACTGCCTTTAATTAACATAATATTAACTTTTGCTGAGGTT TATGAGATTTTCTCACCCCACATCGCTCCCCTTTTTTTAAAAAGGACTGTTTTGCTAGTG TGATAATGAATAGGTAAGATATGAGATAATTGCAACATTGTCCTAGTTCTAGTATGGTAA

### FIGURE 2G

CTATTCTTGAAATGGTATTGAAAAATACCGTTAATTCAAATTGACAGAGATTGATAAAAA TCCCTCATTCTTATTACCAGAAAGAGCTTGCAAATAGTTTTACTTTCTTGGCACTGGAAG GGTAGTTCTGGAAAGCTACTTTGTTGAGAGTCTCATTCTTCCCTGGAGTTAATAGAGTGA TTCACAATCTTTGGGGTTTTCTCCTCATCAAAAGCATTTCTTAAGTGCCTATCTAAAAGC AATTAAAGACTGTGTCTGCCCTTTAGAAGCTAAGAATTTGATTCATGATGCAAATTAACT AGATAATTTGCAAAGTACCCTTGAGATTGAATTTTCTCTATTATATATTTCCCATATTTC AGGTGAATAATTTAATTTAAATGACAAAACCCTATCTAGTCAACTGGGCATAATGACATT TTCTTTAAATTAGACTCTATTTTGAATTAAAAGAGTTTTATTATAAACCGTGTGTTTTTTG GTTTTTCTAAGTATATAGAAAGCTTGTATAATTCAGATTTATCAATTTCCTGATTTAATG TAGACTTTGACTTTTTATTAAAAACCTTTGTATTAAAGCAAGTTATGTTATTTTCTTT TATGCATTTATTACTAACATAGCTTTAAATCTTTAAATGTATTGAAGCATTGTGCTGTCT GAAAATAAGGAATTGCTTATAAACCAGCCACTTCTGAATACAATATGTAGCTGATTTAAT GCCTAAGATAGGGTTTCATTTATTTCTATACTTTTTCTGTTTTTTAAACACCTGCATATT ATAAAACCTTAGACAATCAATCAGTCAGTCTTTACTGACAGGAGCAGCAGCTATCTGTCT TTTGCTGATCTACAAATAAATGAATTGAGAATTTAGTCCATAGAGGTCCCTGGCTACCAA ACACATTCTCCTTTGAATTGTTAAAATTCAGAACATTCAAAATAACTGTTTTGCTACAAC CCATGATTATTTCCTGTTGTGTTTATTTAAATTTACTTTCTCTTTAGAAGTGCACTTAT TTCTGAAAAATCTTAATGAAACAAACGCTTAGAACAAATATAAATATGAGACACTTGGGA CTACTAGAGATATTTTAGATTTTTATGAAAAAAATGTGAGGGGATATTGCTGCTTTAAAA AGGAATAAAGTAATAAAAATATATCTCAGCTATTTTTTTAAAGCAATATAATTCAGCAAT TGTCTAGAAAAGTAATCATGAGGCTACTGAGTTTGGTGTTCAGTTACTGAGTTTCAAAAA TGTTTTGGTGGCATGAGGACAAAATTTCATTGAAGGTAAGATAAGAATAAAAACTATGTT TAC

SEQ ID NO: 9 AA210825 H CGCCCCTTCCTCACGGCTCCCGACCGAACTTTTCTCCAACTTCTGCGACTCGTGAGATT CCCTTCTACCCACTCCGGCCCTCGGGACCCCTCTGCCCATCCCCTGGCCGGTCGGGTCCC TGCGAACCCCTTTATCTCTGGAATCCACTCGGTCCCCGACTCAGAGACTCCTGCCCTCCA CCCCCAAGGACCCCGCCATCCTCAGGTCCCCTCCGCCTGCCAGATCTTTTCTCGGATCCC CGCTCTCCCACCACCTGCTCACGAGATCCCGCGGATCTAGAACCCAGGGTCCCCCGGGGC CCCCGGCGGTCCCGGGTGGGCTCCAGGCGGGCGTCCCCGGCCTCCCCATGGCCAC CCGGCGGCCTAGAGCTGCAGTCGCCGCCACCGCTACTGCCCCAGATCCCGGCCCCGGGTT CCGGGGTCTCCTTTCACATCCAGATCGGGCTGACCCGCGAGTTCGTGCTGTTGCCCGCCG CCTCCGAGCTGGCTCATGTGAAGCAGCTGGCCTGTTCCATCGTGGACCAGAAGTTCCCTG AGTGTGGCTTCTACGGCCTTTACGACAAGATCCTGCTTTTCAAACATGACCCCACGTCGG CCAACCTCCTGCAGCTGGTGCGCTCGTCCGGAGACATCCAGGAGGGCGACCTGGTGGAGG TGCACTCCTATCGGGCGCCTGCCTTCTGTGATCACTGCGGGGAGATGCTCTTCGGCCTAG TGCGCCAGGGCCTCAAGTGCGATGGCTGCGGGCTGAACTACCACAAGCGCTGTGCCTTCA GCATCCCCAACAACTGTAGTGGGGCCCGCAAACGGCGCCTGTCATCCACGTCTCTGGCCA GTGGCCACTCGGTGCGCCTCGGCACCTCCGAGTCCCTGCCCTGCACGGCTGAAGAGCTGA CCTCATCGTATACGGGCCGCCCCATTGAGCTGGACAAGATGCTGCTCTCCAAGGTCAAGG TGCCGCACACCTTCCTCATCCACAGCTATACACGGCCCACCGTTTGCCAGGCTTGCAAGA AACTCCTCAAGGGCCTCTTCCGGCAGGGCCTGCAATGCAAAGACTGCAAGTTTAACTGTC

#### FIGURE 2H

ACAAACGCTGCGCCACCCGCGTCCCTAATGACTGCCTGGGGGAGGCCCTTATCAATGGAG ATGTGCCGATGGAGGAGGCCACCGATTTCAGCGAGGCTGACAAGAGCGCCCTCATGGATG AGTCAGAGGACTCCGGTGTCATCCCTGGCTCCCACTCAGAGAATGCGCTCCACGCCAGTG AGGAGGAGGAGGCGAGGGAGGCCAGAGCTCCCTGGGGTACATCCCCCTAATGA GGGTGGTGCAATCGGTGCGACACACGACGCGGAAATCCAGCACCACGCTGCGGGAGGGTT GGGTGGTTCATTACAGCAACAAGGACACGCTGAGAAAGCGGCACTATTGGCGCCTGGACT GCAAGTGTATCACGCTCTTCCAGAACAACACGACCAACAGATACTATAAGGAAATTCCGC TGTCAGAAATCCTCACGGTGGAGTCCGCCCAGAACTTCAGCCTTGTGCCGCCGGGCACCA ACCCACACTGCTTTGAGATCGTCACTGCCAATGCCACCTACTTCGTGGGCGAGATGCCTG GCGGGACTCCGGGTGGGCCAAGTGGGCAGGGGGCTGAGGCCGCCCGGGGGCTGGNNGAGA CAGCCATCCGCCAGGCCCTGATGCCCGTCATCCTTCAGGACGCACCCAGCGCCCCAGGCC ACGCGCCCACAGACAAGCTTCTCTGAGCATCTCTGTGTCCAACAGTCAGATCCAAGAGA ATGTGGACATTGCCACTGTCTACCAGATCTTCCCTGACGAAGTGCTGGGCTCAGGGCAGT TTGGAGTGGTCTATGGAGGAAAACACCGGAAGACAGGCCGGGACGTGGCAGTTAAGGTCA TTGACAAACTGCGCTTCCCTACCAAGCAGGAGAGCCAGCTCCGGAATGAAGTGGCCATTC TGCAGAGCCTGCGGCATCCCGGGATCGTGAACCTGGAGTGCATGTTCGAGACGCCTGAGA AAGTGTTTGTGGTGATGGAGAAGCTGCATGGGGACATGTTGGAGATGATCCTGTCCAGTG AGAAGGGCCGGCTGCCTGAGCGCCTCACCAAGTTCCTCATCACCCAGATCCTGGTGGCTT TGAGACACCTTCACTTCAAGAACATTGTCCACTGTGACTTGAAACCAGAAAACGTGTTGC TGGCATCAGCAGACCCATTTCCTCAGGTGAAGCTGTGTGACTTTGGCTTTGCTCGCATCA TCGGCGAGAAGTCGTTCCGCCGCTCAGTGGTGGCACGCCGGCCTACCTGGCACCCGAGG TGCTGCTCAACCAGGGCTACAACCGCTCGCTGGACATGTGGTCAGTGGGCGTGATCATGT ACGTCAGCCTCAGCGGCACCTTCCCTTTCAACGAGGATGAGGACATCAATGACCAGATCC AGAACGCCGCCTTCATGTACCCGGCCAGCCCCTGGAGCCACATCTCAGCTGGAGCCATTG ACCTCATCAACAACCTGCTGCAGGTGAAGATGCGCAAACGCTACAGCGTGGACAAATCTC TCAGCCACCCTGGTTACAGGAGTACCAGACGTGGCTGGACCTCCGAGAGCTGGAGGGGA AGATGGGAGAGCGATACATCACGCATGAGAGTGACGACGCGCGCTGGGAGCAGTTTGCAG CAGAGCATCCGCTGCCTGGGTCTGGGCTGCCCACGGACAGGGATCTCGGTGGGGCCTGTC CACCACAGGACCACGACATGCAGGGGCTGGCGGAGCGCATCAGTGTTCTCTGAGGTCCTG TGCCCTCGTCCAGCTGCTCCCACAGCGGTTCTTCACAGGATCCCAGCAATGAACTG TTCTAGGGAAAGTGGCTTCCTGCCCAAACTGGATGGGACACGTGGGGAGTGGGGTGGGGG GAGCTATTTCCAAGGCCCCTCCCTGTTTCCCCAGCAATTAAAACGGACTCATCTCTGGCC CCATGGCCTTGATCTCAGCAAAA

SEQ ID NO: 11\_AA316804\_H
ATGTCTGCAAATAATTCCCCTCCATCAGCCCAGAAGTCTGTATTACCCACAGCTATTCCT
GCTGTGCTTCCAGCTGCTTCTCCGTGTTCAAGTCCTAAGACGGGACTCTCTGCCCGACTC
TCTAATGGAAGCTTCAGTGCACCATCACTCACCAACTCCAGAGGCTCAGTGCATACAGTT
TCATTTCTACTGCAAATTGGCCTCACACGGGAGAGTGTTACCATTGAAGCCCAGGAACTG
TCTTTATCTGCTGTCAAGGATCTTGTGTGCTCCATAGTTTATCAAAAGTTTCCAGAGTGT
GGATTCTTTGGCATGTATGACAAAATTCTTCTCTTTTCGCCATGACATGAACTCAGAAAAC
ATTTTGCAGCTGATTACCTCAGCAGATGAAATACATGAAGGAGACCTAGTGGAAGTGGTT

### FIGURE 2I

CTTTCAGCTTTAGCCACAGTAGAAGACTTCCAGATTCGTCCACATACTCTCTATGTACAT TCTTACAAAGCTCCTACTTTCTGTGATTACTGTGGTGAGATGCTGTGGGGATTGGTACGT CAAGGACTGAAATGTGAAGGCTGTGGATTAAATTACCATAAACGATGTGCCTTCAAGATT CCAAATAACTGTAGTGGAGTAAGAAAGAGACGTCTGTCAAATGTATCTTTACCAGGACCC GGCCTCTCAGTTCCAAGACCCCTACAGCCTGAATATGTAGCCCTTCCCAGTGAAGAGTCA CATGTCCACCAGGAACCAAGTAAGAGAATTCCTTCTTGGAGTGGTCGCCCAATCTGGATG GAAAAGATGGTAATGTGCAGAGTGAAAGTTCCACACACATTTGCTGTTCACTCTTACACC CGTCCCACGATATGTCAGTACTGCAAGCGGTTACTGAAAGGCCTCTTTCGCCAAGGAATG CAGTGTAAAGATTGCAAATTCAACTGCCATAAACGCTGTGCATCAAAAGTACCAAGAGAC TGCCTTGGAGAGGTTACTTTCAATGGAGAACCTTCCAGTCTGGGAACAGATACAGATATA CCAATGGATATTGACAATAATGACATAAATAGTGATAGTAGTCGGGGTTTGGATGACACA GAAGAGCCATCACCCCCAGAAGATAAGATGTTCTTCTTGGATCCATCTGATCTCGATGTG GAAAGAGATGAAGAAGCCGTTAAAACAATCAGTCCATCAACAAGCAATAATATTCCGCTA ATGAGGGTTGTACAATCCATCAAGCACACAAAGAGGAAGAGCAGCACAATGGTGAAGGAA GGGTGGATGGTCCATTACACCAGCAGGGATAACCTGAGAAAGAGGCATTATTGGAGACTT GACAGCAAATGTCTAACATTATTTCAGAATGAATCTGGATCAAAGTATTATAAGGAAATT CCACTTCAGAAATTCTCCGCATATCTTCACCACGAGATTTCACAAACATTTCACAAGGC AGCAATCCACACTGTTTTGAAATCATTACTGATACTATGGTATACTTCGTTGGTGAGAAC AATGGGGACAGCTCTCATAATCCTGTTCTTGCTGCCACTGGAGTTGGACTTGATGTAGCA TGCACTTCTCCAGGGCAAGGGAAAGATCACAAAGATTTGTCTACAAGTATCTCTGTATCT AATTGTCAGATTCAGGAGAATGTGGATATCAGTACTGTTTACCAGATCTTTGCAGATGAG GTGCTTGGTTCAGGCCAGTTTGGCATCGTTTATGGAGGAAAACATAGAAAGACTGGGAGG GATGTGGCTATTAAAGTAATTGATAAGATGAGATTCCCCACAAAACAAGAAAGTCAACTC CGTAATGAAGTGGCTATTTTACAGAATTTGCACCATCCTGGGATTGTAAACCTGGAATGT ATGTTTGAAACCCCAGAACGAGTCTTTGTAGTAATGGAAAAGCTGCATGGAGATATGTTG GAAATGATTCTATCCAGTGAGAAAAGTCGGCTTCCAGAACGAATTACTAAATTCATGGTC ACACAGATACTTGTTGCTTTGAGGAATCTGCATTTTAAGAATATTGTGCACTGTGATTTA AAGCCAGAAAATGTGCTGCTTGCATCAGCAGAGCCATTTCCTCAGGTGAAGCTGTGTGAC TTTGGATTTGCACGCATCATTGGTGAAAAGTCATTCAGGAGATCTGTGGTAGGAACTCCA GCATACTTAGCCCCTGAAGTTCTCCGGAGCAAAGGTTACAACCGTTCCCTAGATATGTGG TCAGTGGGAGTTATCATCTATGTGAGCCTCAGTGGCACATTTCCTTTTAATGAGGATGAA GATATAAATGACCAAAATCCAAAATGCTGCATTTATGTACCCACCAAATCCATGGAGAGAA ATTTCTGGTGAAGCAATTGATCTGATAAACAATCTGCTTCAAGTGAAGATGAGAAAACGT TACAGTGTTGACAAATCTCTTAGTCATCCCTGGCTACAGGACTATCAGACTTGGCTTGAC CTTAGAGAATTTGAAACTCGCATTGGAGAACGTTACATTACACATGAAAGTGATGATGCT CGCTGGGAAATACATGCATACACATAACCTTGTATACCCAAAGCACTTCATTATGGCT CCTAATCCAGATGATATGGAAGAAGATCCTTAA

SEQ ID NO: 12\_PKNBETA\_H
ATGGAGGGGGGGCGCGCGGCAGCCTGGGCCGAGCCAGTGGCCCCAGAGGATGAGAAG
GAGGTGATCCGCCGGGCCATCCAGAAAGAGCTGAAGATCAAGGAGGGGGTGGAGAACCTG
CGGCGCGTGGCCACAGACCGCCGCCACTTGGGCCATGTGCAGCAGCTGCTGCGGTCCTCC
AACCGCCGCCTGGAGCAGCTGCATGGCGAGCTGCGGGAGCTGCACGCCCGAATCCTGCTG
CCCGGCCCTGGGCCTGGCCCAGCTGAGCCTGTGGCCTCAGGACCCCGGCCGTGGGCAGAG
CAGCTCAGGGCTCGGCACCTAGAGGCTCTCCGGAGGCAGCTGCATGTGGAGCTGAAGGTG
AAACAGGGGGCTGAGAACATGACCCACACGTGCGCCAGTGGCACCCCCAAGGAGAGAAG
CTCCTTGCAGCTGCCCAGCAGATGCTCCCGGAGCCAGCTGAAGGTGGCCCTGCTGCGG
ATGAAGATCAGCAGCCTGGAGGCCAGTTGAGGCCCCCAAGAACCTG

PCT/US00/14842

#### FIGURE 2J

GTGAAACTGCTTAGTAGCCGGAGAACACAGGACCGCAAGGCACTGGCTGAGGCCCAGGCC CAGCTACAGGAGTCCTCTCAGAAACTGGACCTCCTGCGCCTTGGAGCAGCTGCTG GAGCAACTGCCTCCTGCCCACCCTTTGCGCAGCAGAGTGACCCGAGAGTTGCGGGCTGCG GTGCCTGGATACCCCCAGCCTTCAGGGACACCTGTGAAGCCCACCGCCCTAACAGGGACA CTGCAGGTCCGCCTCCTGGGCTGTGAACAGTTGCTGACAGCCGTGCCTGGGCGCTCCCCA GCGGCCGCACTGGCCAGCAGCCCCTCCGAGGGCTGGCTTCGGACCAAGGCCAAGCACCAG CGTGGCCGAGGCGAGCTTGCCAGTGAGGTGCTGGCTGTGCTAAAGGTGGACAACCGTGTT GTGGGGCAGACGGCTGGGGGCAGGTGGCCGAACAGTCCTGGGACCAGACCTTTGTCATC CCACTGGAGCGAGCCCGTGAGCTGGAGATTGGGGTACACTGGCGGGACTGGCGGCAGCTA TGTGGCGTGGCCTTCCTGAGACTTGAAGACTTCCTGGACAATGCCTGTCACCAACTGTCC CTCAGCCTGGTACCGCAGGGACTGCTTTTTGCCCAGGTGACCTTCTGCGATCCTGTCATT GAGAGGCGGCCCGGCTGCAGAGGCAGGAACGCATCTTCTCTAAACGCAGAGGCCAGGAC TTCCTGAGGCGTTCGCAGATGAACCTCGGCATGGCGGCCTGGGGGGCCCTCGTCATGAAC CTGCTGCCCCCTGCAGCTCCCCGAGCACAATCAGCCCCCTAAAGGATGCCCTCGGACC CCAACAACACTGCGAGAGGCCTCTGACCCTGCCACTCCCAGTAATTTCCTGCCCAAGAAG ACCCCTTGGGTGAAGAGATGACACCCCCACCCAAGCCCCACGCCTCTACCTCCCCAG GAGCCAACATCCGAGGAGACTCCGCGCACCAAACGTCCCCATATGGAGCCTAGGACTCGA CGTGGGCCATCTCCACCAGCCTCCCCACCAGGAAACCCCCTCGGCTTCAGGACTTCCGC TGCTTAGCTGTGCTGGGCCGGGGACACTTTGGGAAGGTCCTCCTGGTCCAGTTCAAGGGG ACAGGGAAATACTACGCCATCAAAGCACTGAAGAAGCAGGAGGTGCTCAGCCGGGACGAG ATAGAGAGCCTGTACTGCGAGAAGCGGATCCTGGAGGCTGTGGGCTGCACAGGGCACCCT TTCCTGCTCTCCTTGTCTGCTTCCAGACCTCCAGCCATGCCCGCTTTGTGACTGAG TTTGTGCCTGGTGGTGACCTCATGATGCAGATCCACGAGGATGTCTTCCCCGAGCCCCAG GCCCGCTTCTACGTGGCTTGTGTTGTCCTGGGGCTGCAGTTCTTACACGAGAAGAAGATC ATTTACAGGGACCTGAAGTTGGATAACCTTCTGCTGGATGCCCAGGGATTCCTGAAGATC GCAGACTTTGGACTCTGCAAGGAAGGGATCGGCTTCGGGGACCGGACTAGCACCTTCTGT GGCACCCGGAGTTCCTGGCTCCCGAGGTGCTGACCCAGGAGGCATACACACAGGCCGTC GGGGACACAGAGGAAGAGTGTTTGACTGCATCGTCAACATGGACGCCCCCTACCCCGGC TTTCTGTCGGTGCAAGGGCTTGAGTTCATTCAGAAGCTCCTCCAGAAGTGCCCGGAGAAG CGCCTCGGGGCAGGTGAGCAGGATGCCGAGGAGATCAAGGTCCAGCCATTCTTCAGGACC ACCAACTGGCAAGCCCTGCTCGCCCGCACCATCCAGCCCCCTTCGTGCCTACCCTGTGT GGCCCTGCGGACCTGCGCTACTTTGAGGGCGAGTTCACAGGGCTGCCGCCTGCCCTGACC CCACCTGCACCCCACAGCCTCCTCACTGCCCGCCAACAGGCCGCCTTCCGGGACTTCGAC TTTGTGTCAGAGCGATTCCTGGAACCCTGA

SEQ ID NO: 13\_AI021023\_M PKNBETA\_M

GCTGAAGTGGGATAACCTTCTGCTGGATGCCCAGGGATTCCTGAAGATCGCAGACTTTGG
ACTCTGCAAGGAAGGGATCGGCTTCGGGGACCGGACTAGCACCTTCTGTGGCACCCCGGA
GTTCCTGGCTCCCGAGGTGCTGACCCAGGAGGCATACACACGGGCTGTGGACTGGTGGGG
GCTGGGTGTGCTCTACGAGATGCTGGTGGTGAGTGCCCGTTCCCAGGGGACACAGA
GGAAGAGGTGTTTGACTGCATCGTCAACATGGACGCCCCCTACCCCGGCTTTCTGTCGGT
GCAAGGGCTTGAGTTCATTCAGAAGCTCCTCCAGAAGTGCCCGGAGAAGCGCCTCGGGGC
GGGTGAGCAGGATGCCGAGGAGATCAAGGTCCAGCCATTCTTCAGGACCACCAACTGGCA
AGCCCTGCTCGCCCGCACCATCCAGCCCCCCTTTGTGCCTACCCTGTGTGGCCCTGCCGGA
CCTGCGCTACTTTGAGGGCGAGTTCACAGGGCTGCCGCCTGCCCTGACCCCACCTGCAC
CCACAGCCTCCTCACTGCCCGCCAACAGGCCGCCTTCCGGGACTTCGACTTTGTGTCAGA
GCGATTCCTGGAACCCTGAGGGCATCTCCTGGCACCTTCCCCCACAGACTG
TTAGAGCCTCTGCTCGTTCACCCGTGCGCCCTGCCTGGAGCCTTTCCTGGGTAC
TTCTGAGCCCTTGGGATTCAAAGTGGCAGCCATGGGGCCACTGTTGTGGGCTTTGCTCAG

# FIGURE 2K

TGTCACTGGGCAAAGTGTGTCCCTTCCCCCTCCAGCTCGCCCTCTTCTACCTCCCAGCGA GACCTGGCCCAGAAAGGGTGCCGCAGCAAGGAGTGATATGGTTTGTCTTTTTAAGACTGG ACTTGCTTTATATTAAATTTGTAAAAGTG

SEQ ID NO: 14 H19102 H GGTGGCAACATCCGGGGTCCCTGGGCCCGAGGCTGGAAGAGCCTCTGGACAGGTTTGGGA ACCATCAGGTCAGATCTGGAAGAACTCTGGGAACTACGGGGGCACCACTATCTGCACCAG GAATCCCTAAAGCCAGCCCCAGTACTGGTAGAGAAGCCTCTGCCAGAGTGGCCAGTGCCT CAGTTCATCAACCTCTTTCTACCAGAGTTTCCCATTAGGCCCATTAGGGGGCCAGCAG CTGAAGATTTTAGGCCTCGTGGCTAAAGGCTCCTTTGGAACTGTCCTCAAGGTGCTAGAT TGCACCCAGAAAGCTGTATTTGCAGTGAAGGTGCCCCAAGGTAAAGGTCCTACAGAGG GATACCGTGAGGCAGTGCAAAGAGGAGGTTAGCATCCAGCGACAGATCAACCATCCCTTT GTACACAGCTTGGGGGACAGCTGGCAGGGAAAACGGCACCTTTTCATTATGTGTAGCTAC TGCAGCACAGATCTGTACTCCCTTTGGTCGGCTGTTGGCTGCTTTCCTGAGGCTTCCATC CGTCTCTTTGCTGCCGAGTTGGTGCTGGTACTGTGTTATCTCCATGACTTGGGCATCATG CATCGAGATGTGAAGATGGAGAATATTCTTCTAGATGAACGAGGCCATCTGAAACTGACA GACTTTGGTCTGTCCCGCCACGTGCCCCAGGGAGCTCAAGCCTACACTATCTGTGGCACT CTTCAGTACATGGCCCCAGAGGTCCTAAGTGGAGGACCTTACAACCATGCTGCTGATTGG TGGTCCCTGGGTGTCTTGCTTTTCTCTCTGGCGACTGGAAAGTTTCCAGTGGCTGCAGAG AGAGATCATGTGGCCATGTTGGCAAGTGTGACCCACAGTGACTCTGAGATCCCAGCTTCT CTTAACCAGGGCCTCTCACTCCTGCTCCATGAGCTCTTATGCCAGAACCCCCTCCATCGT GAGCTCCTACAGAAGCAGCCAGTGAACTTTGTCACGGAGACACAAGCTACCCAGCCCAGT TCAGCGGAGACCATGCCCTTTGACGACTTTGACTGTGATCTGGAGTCCTTCTTGCTCTAC CCTATCCCTGCTTGA

SEO ID NO: 15 AA476563\_H  $\overline{\text{ATGGAATTCTTTAGGATAGACAGTAAGGATAGCGCAAGTGAACTCCTGGGACTTGACTTT}$ GGAGAAAATTGTATAGTCTAAAATCAGAACCTTTGAAACCATTCTTTACTCTTCCAGAT GGAGACAGTGCTTCTAGGAGTTTTAATACTAGTGAAAGCAAGGTAGAGTTTAAAGCTCAG GACACCATTAGCAGGGGCTCAGATGACTCAGTGCCAGTTATTTCGTTTAAAGATGCTGCT TTTGATGATGTCAGTGGTACTGATGAAGGAAGACCTGATCTTCTTGTAAATTTACCTGGT GAATTGGAGTCAACAAGAGAAGCTGCAGCAATGGGACCTACTAAGTTTACACAAACTAAT ATAGGGATAATAGAAAATAAACTCTTGGAAGCCCCTGATGTTTTATGCCTCAGGCTTAGT ACTGAACAATGCCAAGCACATGAGGAGAAAGGCATAGAGGAACTGAGTGATCCCTCTGGG CCCAAATCCTATAGTATAACAGAGAAACACTATGCACAGGAGGATCCCAGGATGTTATTT GTAGCAGCTGTTGATCATAGTAGTTCAGGAGATATGTCTTTGTTACCCAGCTCAGATCCT AAGTTTCAAGGACTTGGAGTGGTTGAGTCAGCAGTAACTGCAAACAACACAGAAGAAAGC TTATTCCGTATTTGTAGTCCACTCTCAGGTGCTAATGAATATATTGCAAGCACAGACACT TTAAAAACAGAAGAAGTATTGCTGTTTACAGATCAGACTGATGATTTGGCTAAAGAGGAA CCAACTTCTTTATTCCAGAGAGACTCTGAGACTAAGGGTGAAAGTGGTTTAGTGCTAGAA GGAGACAAGGAAATACATCAGATTTTTGAGGACCTTGATAAAAAATTAGCACTAGCCTCC AGGTTTTACATCCCAGAGGGCTGCATTCAAAGATGGCAGCTGAAATGGTGGTAGCCCTT GATGCTTTACATAGAGAGGGAATTGTGTGCCGCGATTTGAACCCAAACAACATCTTATTG AATGATAGAGGACACATTCAGCTAACGTATTTTAGCAGGTGGAGTGAGGTTGAAGATTCC TGTGACAGCGATGCCATAGAGAGATGTACTGTGCCCCAGAGGTTGGAGCAATCACTGAA GAAACTGAAGCCTGTGATTGGTGGAGTTTGGGTGCTGTCCTCTTTGAACTTCTCACTGGC AAGACTCTGGTTGAATGCCATCCAGCAGGAATAAATACTCACACTACTTTGAACATGCCA GAATGTGTCTCTGAAGAGGCTCGCTCACTCATTCAACAGCTCTTGCAGTTCAATCCTCTG

PCT/US00/14842

# FIGURE 2L

GAACGACTTGGTGCTGGAGTTGCTGGTGTTGAAGATATCAAATCTCATCCATTTTTTACCCCTGTGGATTGGGCAGAACTGATGAGATGA

SEQ ID NO: 16 AA626690 H

ATGCTACCATTCGCTCCTCAGGACGAGCCCTGGGACCGAGAAATGGAAGTGTTCAGCGGC GGCGCGCGAGCAGCGAGGTAAATGGTCTTAAAATGGTTGATGAGCCAATGGAAGAG GGAGAAGCAGATTCTTGTCATGATGAAGGAGTTGTTAAAGAAATCCCTATTACTCATCAT GTTAAGGAAGGCTATGAGAAAGCAGATCCTGCACAGTTTGAGTTGCTCAAGGTTCTTGGT CAGGGGTCATTTGGAAAGGTTTTTCTTGTTAGAAAGAAGACCGGTCCTGATGCTGGGCAG CTCTATGCAATGAAGGTGTTAAAAAAAGCCTCTTTAAAAGTTCGAGACAGAGTTCGGACA AAGATGGAGAGGGATATACTGGTGGAAGTAAATCATCCATTTATTGTCAAATTGCACTAT GCCTTTCAGACTGAAGGGAAACTGTACTTAATACTGGATTTTCTCAGGGGAGGAGATGTT TTCACAAGATTATCCAAAGAGGTTCTGTTTACAGAGGAAGATGTGAAATTCTACCTCGCA GAACTGGCCCTTGCTTTGGATCATCTGCACCAATTAGGAATTGTTTATAGAGACCTGAAG CCAGAAAACATTTTGCTTGATGAAATAGGACATATCAAATTAACAGATTTTTGGACTCAGC AAGGAGTCAGTAGATCAAGAAAAGAAGGCTTACTCATTTTGTGGTACAGTAGAGTATATG GCTCCTGAAGTAGTAAATAGGAGAGGCCATTCCCAGAGTGCTGATTGGTGGTCATATGGT GTTCTTATGTTTGAAATGCTTACTGGTACTCTGCCATTTCAAGGTAAAGACAGAAATGAG ACCATGAATATGATATTAAAAGCAAAACTTGGAATGCCTCAATTTCTTAGTGCTGAAGCA CAAAGTCTTCTAAGGATGTTATTCAAAAGGAATCCAGCAAATAGATTGGGATCAGAAGGA GTTGAAGAAATCAAAAGACATCTGTTTTTTGCAAATATTGACTGGGATAAATTATATAAA AGAGAAGTTCAACCTCCTTTCAAACCTGCTTCTGGAAAACCAGATGATACTTTTTGTTTT GCTCATCAGCTCTTCAAAGGATTCAGCTTTGTTGCAACTTCTATTGCAGAAGAATATAAA ATCACTCCTATCACAAGTGCAAATGTATTACCAATTGTTCAGATAAATGGAAATGCTGCA CAATTTGGTGAAGTATATGAATTGAAGGAGGATATTGGTGTTTGGCTCCTACTCTGTTTGC AAGCGATGCATACATGCAACTACCAACATGGAATTTGCAGTGAAGATCATTGACAAAAGT AAGCGAGACCCTTCAGAAGAGATTGAAATATTGATGCGCTATGGACAACATCCCAACATT ATTACTTTGAAGGATGTCTTTGATGATGGTAGATATGTTTACCTTGTTACGGATTTAATG AAAGGAGGAGAGTTACTTGACCGTATTCTCAAACAAAAATGTTTCTCGGAACGGGAGGCT AGTGATATACTATATGTAATAAGTAAGACAGTTGACTATCTTCATTGTCAAGGAGTTGTT CATCGTGATCTTAAACCTAGTAATATTTTATACATGGATGAATCAGCCAGTGCAGATTCA ATCAGGATATGTGATTTTGGGTTTGCAAAACAACTTCGAGGAGAAAATGGACTTCTCTTA ACTCCATGCTACACTGCAAACTTTGTTGCACCTGAGGTTCTTATGCAACAGGGATATGAT CCATTTGCTAATGGCCCCAATGATACTCCTGAAGAGATACTGCTGCGTATAGGCAATGGA AAATTCTCTTTGAGTGGTGGAAACTGGGACAATATTTCAGACGGAGCAAAGGATTTGCTT TCCCATATGCTTCATATGGACCCACATCAGCGGTATACTGCTGAACAAATATTAAAGCAC TCATGGATAACTCACAGAGACCAGTTGCCAAATGATCAGCCAAAGAGAAATGATGTGTCA CATGTTGTTAAGGGAGCAATGGTTGCAACATACTCTGCCCTGACTCACAAGACCTTTCAA CCAGTCCTAGAGCCTGTAGCTGCTTCAAGCTTAGCCCAGCGACGGAGCATGAAAAAGCGA ACATCAACTGGCCTGTAA

SEQ ID NO: 17 AA215680 H

# FIGURE 2M

CCGCTGAGCAGTGGAGCCAGCCCCAGCGCGGGTTTCAGCAGCCTGAGGCTCCGGCCCATT CGCACGCTGAGCTCTGCCGTGGAGCAGCTGAGGGGCTGCAGGGTGGTCGGGGTCATCGAG AAGGTGCAGCTGGTCCAGGACCCGGCAACCGGAGGGACCTTTGTGGTGAAGAGCCTACCC AGGTGCCACATGGTGAGCAGGGAGCGGCTGACCATCATCCCACACGGAGTCCCCTACATG ACGAAGCTGCTCAGGTACTTTGTGAGCGAGGACTCCATCTTCCTGCACCTGGAGCATGTG CAAGGAGGCACTCTCTGGTCCCACCTGCTCTCCCAGGCGCACTCCCGACATTCTGGGCTC AGCTCTGGCTCTACCCAGGAGAGGATGAAGGCTCAGCTCAACCCCCACCTCAACCTCCTG-ACCCCAGCGAGGCTTCCCTCAGGCCATGCCCCTGGCCAGGACAGAATCGCCCTGGAGCCT CCTAGGACTTCTCCGAACCTTCTCCTAGCTGGGGAGGCCCCATCCACCAGACCCCAGAGG GAGGCTGAAGGTGAACCCACAGCCAGGACCAGCACCTCTGGCTCCTCGGACCTTCCAAAG GCCCCAGGTGGCCACCTGCACCTTCAAGCTAGGAGGGCTGGCCAGAACTCAGACGCTGGG CCCCTCGGGGGCTCACTTGGGTTCCTGAGGGGGCCCGGCCCGGTGCTAGGGGGCTGTGGC ACCTGGAGTGTGAGAGGAGCAGGTGAAGCAGTGGGCGGCAGAGATGCTGGTAGCGCTG GAGGCGCTGCACGAGCAGGGGGTGCTGTGCCGGGACCTCCACCCCGGGAACCTGCTCCTG GACCAGGCAGGTCACATCCGGCTCACATATTTTGGCCAGTGGTCAGAGGTGGAGCCCCAG CTGACGGAAGCCTGTGACTGGGGGCTTTGGGTCTCTACTGTATGAACTGCTGACGGGA ATGGCACTGTCCCAGAGCCACCCTTCAGGAATCCAGGCCCACACCCAGCTCCAGCTGCCC GAGTGGCTCAGTCGCCCAGCGGCCTCTCTGCTGACTGAGCTGCTGCAGTTCGAGCCTACC CGGCGCCTGGGCATGGGAGAAGGTGGTGTCAGCAAACTCAAGTCCCATCCCTTTTTCAGT ACCATCCAATGGAGCAAGCTGGTGGGGTAA

SEQ ID NO: 18 SGK H  $\overline{\text{ATGACGGTGAAAACTGAGGCTGCTAAGGGCACCCTCACTTACTCCAGGATGAGGGGCATG}$ GTGGCAATTCTCATCGCTTTCATGAAGCAGAGGAGGATGGGTCTGAACGACTTTATTCAG AAGATTGCCAATAACTCCTATGCATGCAAACACCCTGAAGTTCAGTCCATCTTGAAGATC TCCCAACCTCAGGAGCCTGAGCTTATGAATGCCAACCCTTCTCCTCCACCAAGTCCTTCT CAGCAAATCAACCTTGGCCCGTCGTCCAATCCTCATGCTAAACCATCTGACTTTCACTTC TTGAAAGTGATCGGAAAGGCAGTTTTGGAAAGGTTCTTCTAGCAAGACACAAGGCAGAA AAGCATATTATGTCGGAGCGGAATGTTCTGTTGAAGAATGTGAAGCACCCTTTCCTGGTG GGCCTTCACTTCTCTTTCCAGACTGCTGACAAATTGTACTTTGTCCTAGACTACATTAAT GGTGGAGAGTTGTTCTACCATCTCCAGAGGGAACGCTGCTTCCTGGAACCACGGGCTCGT TTCTATGCTGCTGAAATAGCCAGTGCCTTGGGCTACCTGCATTCACTGAACATCGTTTAT AGAGACTTAAAACCAGAGAATATTTTGCTAGATTCACAGGGACACATTGTCCTTACTGAT TTCGGACTCTGCAAGGAGAACATTGAACACAACAGCACAACATCCACCTTCTGTGGCACG CCGGAGTATCTCGCACCTGAGGTGCTTCATAAGCAGCCTTATGACAGGACTGTGGACTGG TGGTGCCTGGGAGCTGTCTTGTATGAGATGCTGTATGGCCTGCCGCCTTTTTATAGCCGA AACACAGCTGAAATGTACGACAACATTCTGAACAAGCCTCTCCAGCTGAAACCAAATATT ACAAATTCCGCAAGACACCTCCTGGAGGGCCTCCTGCAGAAGGACAGGACAAAGCGGCTC GATGATCTCATTAATAAGAAGATTACTCCCCCTTTTAACCCAAATGTGAGTGGGCCCAAC GAGCTACGGCACTTTGACCCCGAGTTTACCGAAGAGCCTGTCCCCAACTCCATTGGCAAG TCCCCTGACAGCGTCCTCGTCACAGCCAGCGTCAAGGAAGCTGCCGAGGCTTTCCTAGGC TTTTCCTATGCGCCTCCCACGGACTCTTTCCTCTGA

SEQ ID NO: 19\_AA107515\_M CGGGTCGACCCACGCGTCCGCCGGTTTCACTGCTCCCCTCAGTCTCTTTTGGGCTCTTTC CGGGCATCGGGACGATGACCGTCAAAGCCGAGGCTGCTCGAAGCACCCTTACCTACTCCA

### FIGURE 2N

GAATGAGGGGAATGGTAGCGATTCTCATCGCTTTTATGAAACAGAGAAGGATGGGCCTGA CCATTTTGAAAATGTCCCATCCTCAGGAGCCGGAGCTTATGAACGCTAACCCCTCTCCTC CGCCAAGTCCCTCTCAACAAATCAACCTGGGTCCGTCCTCCAACCCTCACGCCAAACCCT CCGACTTTCACTTCTTGAAAGTGATCGGAAAGGGCAGTTTTGGAAAGGTTCTTCTGGCTA GGCACAAGGCAGAAGAAGTATTCTATGCAGTCAAAGTTTTACAGAAGAAAGCCATCCTGA AGAAGAAGAGGAGAAGCATATTATGTCAGAGCGGAATGTTCTGTTGAAGAATGTGAAGC ACCCTTTCCTGGTGGGCCTTCACTTCTCATTCCAGACCGCTGACAAGCTCTACTTTGTCC TGGACTACATTAATGGTGGAGAGCTGTTCTACCATCTCCAGAGGGAGCGCTGCTTCCTGG AACCACGGGCTCGATTCTACGCAGCTGAAATAGCCAGTGCCCTGGGCTATCTGCACTCCC TAAACATCGTTTATAGAGACTTAAAACCTGAGAATATTCTCCTAGACTCCCAGGGGCACA TCGTCCTCACTGACNTATTTCAGCTGCGTAGAATCGAGCATAACGGGACAACATCTACCT TCTGTGGCACGCCTGAGTATCTGGCTCCTGAGGTCCTCCATAAGCAGCCGTATGACCGGA CGGTGGACTGGTGTCTTGGGGCTGTCCTGTATGAGATGCTCTACGGCCTGCCCCCGT TTTATAGCCGGAACACGGCTGAGATGTACGACAATATTCTGAACAAGCCTCTCCAGTTGA AACCAAATATTACAAACTCGGCAAGGCACCTCCTGGAAGGCCTCCTGCAGAAGGACCGGA CCAAGAGGCTGGGTGCCAAGGATGACTTTATGGAGATTAAGAGTCATATTTTCTTCTT TAATTAACTGGGATGATCTCATCAATAAGAAGATTACACCCCCATTTAACCCAAATGTGA GTGGGCCCAGTGACCTTCGGCACTTCGATCCCGAGTTTACCGAGGAGCCGGTCCCCAGCT GGTTCTGAAGGACTTCCTCAGCGTTTCCTAAAGTGTTTTCGTTAGCCTTTGGTGGAGTTG CCAGCTGACAGAACATTTTAAAAGAATTTGCACACCTGGAAGCTTGGCAGTCTCGCCTGC CCGGCGTGGCGCGCGCGCGCGCTGCTTGATGGGAGCTTTCCGAAGAGCACACCCTC CTCTCAATGAGCTTGTGAGGTCTTCTTTTTTTTTCTTCTTCCTAACGTGGTGCTAGCTCC ATGCAGGTCTAAGAGGAATCCCCGCAGGTCTGTCTGAGCTGTGATCAAGAATATTCTGCA ATGTGCCTTTTCTGAGATCGTGTTAGCTCCAAAGCTTTTTCCTATCGCAGAGTGTTCAGT TTGTGTTTGTTTTTGTTTTTGTTTTTTCCCTTGGCGGATTTCCCGTGTGCA GTGGCGTGAGTGTGCTATGCCTGATCACAGACGGTTTTGTTGTGAGCATCAATGTGACAC TTGCAGGACACTACAATGTGGGACATTGTTTGTTTCTTCCACATTTGGAAGATAAATTTA TGTGTAGACTGTTTTGTAAGATATAGTTAATAACTAAAACCTATTGAAACGGTCTTGCAA TGACGAGCATTCAGATGCTTAAGGAAAGCATTGCTGCTACAAATATTTCTATTTTTAGAA AGGGTTTTTATGGACCAATGCCCCAGTTGTCAGTCAAAGCCGTTGGTGTTTTCATTGTTT TGCATTCCTGATTATTGTATGTATCGTGTAAAGGAAGTCTGTACATTGGGTTATAACACT AGATATTTAAACTTACAGGCTTATTTGTAAACCATCATTTTAATGTACTGTAATTAACAT CAATTTTGGTTTGCAATAAAATCTTGAAAACT

SEQ ID NO: 20\_AA109508\_M
CCACCTGCAGCGGGAGCGCCGGTTCCTGGAGCCCCGGGCCAGGTTCTACGCTGCAGGT
GGCCAGCGCCATTGGCTACCTGCACTCCCTCAACATCATTTACAGGGATCTGAAACCAGA
GAACATTCTCTTGGACTGCCAGGGACACGTGGTGCTGACGGATTTTGGCCTCTGCAAGGA
AGGTGTAGAGCCTGAAGACACCACATCCACATTCTGTGGTACCCCTGAGTACTTGGCACC
TGAAGTGCTTCGGAAAGAGCCTTATGATCGAGCAGTGGACTGGTGGTGCTTGGGGGCAGT
CCTCTACGAGATGCTCCATGGCCTGCCGCCCTTCTACAGCCAAGATGTATCCCAGATGTA
TGAGAACATTCTGCACCAGCCGCTACAGATCCCCGGAGGCCGGACAGTGGCCGCCTGTGA
CCTCCTGCAAAGCCTTCTCCACAAGGACCAGAGGCAGCGGCTGGGCTCCAAAGCAGACTT
TCTTGAGATTAAGAACCATGTATTCTTCAGCCCCATAAACTGGGATGACCTGTACCACAA

## FIGURE 20

SEQ ID NO: 21\_AA887783\_H  $\hbox{\tt CGGATGCATTINTTGGTGTGCTCTTGAGGGATTAAATGCAAAGAGATCACACCATGGACT}$ ACAAGGAAAGCTGCCCAAGTGTAAGNATTCCCAGCTCCGATGAACACAGAGAGAAAAAAGA AGAGGTTTACTGTTTATAAAGTTCTGGTTTCAGTGGGAAGAAGTGAATGGTTTGTCTTCA CCCTGAAGATTCCTGCCAAGAGAATATTTGGTGATAATTTTGATCCAGATTTTATTAAAC AAAGACGAGCAGGACTAAACGAATTCATTCAGAACCTAGTTAGGTATCCAGAACTTTATA ACCATCCAGATGTCAGAGCATTCCTTCAAATGGACAGTCCAAAACACCAGTCAGATCCAT CTGAAGATGAGGATGAAAGAAGTTCTCAGAAGCTACACTCTACCTCACAGAACATCAÃCC TGGGACCGTCTGGAAATCCTCATGCCAAACCAACTGACTTTGATTTCTTAAAAGTTATTG CTGTCAAAGTGTTACAGAAAAAAATAGTTCTCAACAGAAAAGAGCAAAAACATATTATGG ATGTTGTCTTAACAGATTTTGGGCTTTGTAAAGAAGGAATTGCTATTTCTGACACCACTA CCACATTTTGTGGGACACCAGAGTATCTTGCACCTGAAGTAATTAGAAAACAGCCCTATG ACAATACTGTAGATTGGTGGTGCCTTGGGGCTGTTCTGTATGAAATGCTGTATGGATTGC CTCCTTTTTATTGCCGAGATGTTGCTGAAATGTATGACAATATCCTTCACAAACCCCTAA GTTTGAGGCCAGGAGTGAGTCTTACAGCCTGGTCCATTCTGGAAGAACTCCTAGAAAAAG ACAGGCAAAATCGACTTGGTGCCAAGGAAGACTTTCTTGAAATTCAGAATCATCCTTTTT TTGAATCACTCAGCTGGGCTGACCTTGTACAAAAGAAGATTCCACCACCATTTAATCCTA ATGTGGCTGGACCAGATGATATCAGAAACTTTGACACAGCATTTACAGAAGAAACAGTTC CATATTCTGTGTGTGTATCTTCTGACTATTCTATAGTGAATGCCAGTGTATTGGAGGCAG ATGATGCATTCGTTGGTTTCTCTTATGCACCTCCTTCAGAAGACTTATTTTTGTGAGCAG TTTGCCATTCAGAAACCATTGAGCAAAATAAGTCTATAGATGGGACTGAAACTTCTATTT GTGTGAATATTCAAATATGTATAACTAGTGCCTCATTTTTATATGTAATGATGAAAAAC TATGAAAAATGTATTTCTTCTATGTGCAAGAAAAATAGGGCATTTCAAAGAGCTGTTT TGATTAAAATTTATATTCTTGTTTAATAAGCTTATTTTTAAACAATTTAAAAGCTATTAT TCTTAGCATTAACCTATTTTTAAAGAAACCTTTTTTTGCTATTGACTGTTTTTTCCCTCTA AGTTTACACTAACATCTACCCAAGATAGACTGTTTTTTAACAGTCAATTTCAGTTCAGCT AACATATATTAATACCTTTGTAACTCTTTGCTATGGCTTTTGTTATCACACCAAAACTAT GCAATTGGTACATGGTTGTTTAAGAAGAAACCGTATTTTTCCATGATAAATCACTGTTTG AAATATTTGGTTCATGGTATGATCGAAATGTAAAAGCATAATTAACACATTGGCTGCTAG TTAACAATTGGAATAACTTTATTCTGCAGATCATTTAAGAAGTAACAGGCCGGGCGCGGT GGCTCACGCCTGTAATCCCAGCACTTTGGGAGGCTGAGGCGGGCAGATCACCTGAGGTCA

## FIGURE 2P

GGAGTTGGAGACCAGCCTGACCAACATGGACAAACCCCGTCTCTACTAAAAATACAAAAT TGGCAGGGTGTGGTGGCACATGCCTATAATCCCAGCTACTTGGGAGGCTAAGGCAGGAGA ATCGCTTGAACCCGGGAGGCGGAGGTTGCAGTGAGCCGAGATCGCACCATTGCACTCCTG CCTGGGCAACAAGAGTGAAACTCCATCTCC

## SEQ ID NO: 22 R47805 H

ATGGCGCACCAAACGGGCATCCACGCCACGGAAGAGCTGAAGGAATTCTTTGCCAAGGCA CGGGCTGGCTCTGTGCGGCTCATCAAGGTTGTGATTGAGGACGAGCAGCTCGTGCTGGGT GCCTCGCAGGAGCCAGTAGGCCGCTGGGATCAGGACTATGACAGGGCCGTGCTGCCACTG CTGGACGCCCAGCAGCCCTGCTACCTGCTCTACCGCCTCGACTCACAGAATGCTCAGGGC TTCGAATGGCTCTTCCTCGCCTGGTCGCCTGATAACTCCCCCGTGCGGCTGAAGATGCTG TACGCGGCCACGCGGCCACAGTGAAAAAGGAGTTTGGAGGTGGCCACATCAAGGATGAG CTCTTCGGGACTGTGAAGGATGACCTCTCTTTTGCTGGGTACCAGAAACACCTGTCGTCC TGTGCGGCACCTGCCCGCTGACCTCGGCTGAGAGAGAGCTCCAGCAGATCCGCATTAAC GAGGTGAAGACAGAGATCAGTGTGGAAAGCAAGCACCAGACCCTGCAGGGCCTCGCCTTC CCCCTGCAGCCTGAGGCCCAGCGGGCACTCCAGCAGCTCAAGCAGAAAATGGTCAACTAC ATCCAGATGAAGCTGGACCTAGAGCGGGAAACCATTGAGCTGGTGCACACAGAGCCCACG GATGTGGCCCAGCTGCCCTCCCGGGTGCCCCGAGATGCTGCCCGCTACCACTTCTTCCTC TACAAGCACACCCATGAGGGCGACCCCCTTGAGTCTGTAGTGTTCATCTACTCCATGCCG GGGTACAAGTGCAGCATCAAGGAGCGAATGCTCTACTCCAGCTGCAAGAGCCGCCTCCTC GACTCCGTGGAGCAGGACTTCCATCTGGAGATCGCCAAGAAAATTGAGATTGGCGATGGG GCAGAGCTGACGGCAGAGTTCCTCTACGACGAGGTGCACCCCAAGCAACACGCCTTCAAG CAGGCCTTCGCCAAGCCCAAGGGCCCAGGGGGCCAAGCGGGCCATAAGCGCCTCATCCGC GGCCCGGGTGAAAATGGGGATGACAGCTAG

# SEQ ID NO: 23 H60215 H

CCACGCGTCCGGCGCGCGCCATGGAGGGAGGCGGCGGCGGCGGCGGCGGCGGCTCGGG TGGCTGCGCTGGGAGGCGGCGGTGAGAGGCTCGCACGCCTCCAGCCCGGCCCCGGCCCCC CGGGAGGGAGAGCCGAGCCCCGGCTCTGGGCTACGGACTATGGGCGAATAGCTCTGA CCACCGGCGAAGTGCACACACCCAGAAGCTATGTCCTTCGGCAGTAAAAGTTTTACAGC ACAATATATGTGCTCTGCTCTCCCGCAATCCTGCTCCAAGAGATCTTAAGCTGGAGG CACCAGGTCTGAATTCCAGACTCCTCCCCACCACCACACTTCACCTCCAACTGGAGCAT GACCACAGACCCATTCAGGGAGGCTGGCGGACTCTTCATCCTGGACAGTCCCTTACTGTA TGTCAAAGCTGAGAATGAAGCGGAGAGCATCAGACAGAGGAGCTGGGGAAACGTCGGCCA GGGCCAAGGCTCTAGGAAGTGGGATTTCTGGAAATAATGCAAAGAGAGCTGGACCATTCA TCCTTGGTCCCCGTCTGGGCAACTCACCGGTGCCAAGCATAGTGCAGTGTTTTGGCGAGGA AAGATGGCACGGATGACTTCTATCAGCTGAAGATCCTGACCCTGGAGGAGGGGGGGACC AAGGCATAGAGAGCCAGGAAGAGCGGCAGGGCAAGATGCTGCACACCCGAGTACTCAC TGCTGTCTCCTGCACACGCAGGATGGCGTGGTGCACCACCACGGCCTCTTCCAGGACC GCACCTGTGAAATCGTTGAGGACACAGAATCCAGCCGGATGGTTAAGAAGATGAAGAAGC GCATCTGCCTCGTCCTGGACTGCCTCTGTGCTCATGACTTCAGCGATAAGACCGCTGACC TCATCAACCTGCAGCACTACGTCATCAAGGAGAAGAGGCTCAGCGAGAGGGAGACTGTGG TAATCTTCTACGACGTGGTCCGCGTGGTGGAGGCCCTGCACCAGAAAATATCGTGCACA GAGACCTGAAGCTGGGGAACATGGTGCTCAACAAGAGGACACATCGGATAACCATCACCA ACTTCTGCCTCGGGAAGCATCTGGTGAGCGAGGGGGACCTGCTGAAGGACCAGAGAGGGA ACATGTGGGCCTGGGCGTGGTGCTCTTCACCATGCTGTATGGCCAGTTCCCCTTCTACG ACAGCATCCCGCAGGAGCTCTTCCGCAAGATCAAGGCTGCCGAGTATACCATTCCTGAGG ATGGACGGGTTTCTGAGAACACCGTGTGTCTCATCCGGAAGCTGCTGGTCCTTGACCCCC AGCAGCGCCTGGCCGCCGACGTCCTGGAGGCCCTCAGTGCCATCATTGCATCATGGC

# FIGURE 2Q

SEO ID NO: 24 SGK324\_H GCCGCGATGGCCAGCACCAGGAGTATCGAGCTGGAGCACTTTGAGGAACGGGACAAAAGG CCGCGGCCGGGGTCGCGGAGAGGGGCCCCCAGCTCCTCCGGGGGCAGCAGCAGCTCGGGC CCCAAGGGGAACGGGCTCATCCCCAGTCCGGCGCACAGTGCCCACTGCAGCTTCTACCGC ACGCGGACCCTGCAGCCCTCAGCTCGGAGAAGAAGGCCCAAGAAGGCGCGCTTCTACCGG AACGGGGACCGCTACTTCAAGGGCCTGGTGTTTGCCATCTCCAGCGACCGCTTCCGGTCC TTCGATGCGCTCCTCATAGAGCTCACCCGCTCCCTGTCGGACAACGTGAACCTGCCCCAG GGTGTCCGCACTATCTACACCATCGACGGCAGCCGGAAGGTCACCAGCCTGGACGAGCTG CTGGAAGGTGAGAGTTACGTGTGCATCCAATGAACCATTTCGTAAAGTCGATTACACC AAAAATATTAATCCAAACTGGTCTGTGAACATCAAGGGTGGGACATCCCGAGCGCTGGCT GCTGCCTCCTGTGAAAAGTGAAGTAAAAGAAAGTAAAGATTTCATCAAACCCAAGTTA GTGACTGTGATTCGAAGTGGAGTGAAGCCTAGAAAAGCCGTGCGGATCCTTCTGAATAAA AAGACTGCTCATTCCTTTGAACAAGTCTTAACAGATATCACCGAAGCCATTAAACNAGCC TCAGGAGTCGTCAAGAGGCTCTGCACCCTGGATGGAAAGCAGGTGAGAGTTACGTGTGTG CATCTGCCAGACTTTTTTGGTGATGACGATGTTTTTATTGCATGTGGACCAGAAAAATTT CGTTATGCCCAAGATGACTTTGTCCTGGATCATAGTGAATGTCGTGTCCTGAAGTCATCT TATTCTCGATCCTCAGCTGTTAAGTATTCTGGATCCAAAAGCCCTGGGCCCTCTCGACGC AGCCAGATTTCTGCTCATGGCAGATCTTCTTCCAATGTAAACGGTGGACCTGAGCTTGAC CGTTGCATAAGTCCTGAAGGTGTGAATGGAAACAGATGCTCTGAATCATCAACTCTTCTT GAGAAATACAAAATTGGAAAGGTCATTGGTGATGGCAATTTTGCAGTAGTCAAAGAGTGT ATAGACAGGTCCACTGGAAAGGAGTTTGCCCTAAAGATTATAGACAAAGCCAAATGTTGT GGAAAGGAACACCTGATTGAGAATGAAGTGTCAATACTGCGCCGAGTGAAACATCCCAAT ATCATTATGCTGGTCGAGGAGATGGAAACAGCAACTGAGCTCTTTCTGGTGATGGAATTG GGCAGTGCCATGGTGTACAACTTAGCCAATGCCCTCAGGTATCTCCATGGCCTCAGCATC GTGCACAGAGACATCAAACCAGAGAATCTCTTGGTGTGTGAATATCCTGATGGAACCAAG TCTTTGAAACTGGGAGACTTTGGGCTTGCGACTGTGGTAGAAGGCCCTTTATACACAGTC TGTGGCACACCCACTTATGTGGCTCCARAAATCATTGCTGAAACTGGCTATGGCCTGAAG GTGGACATTTGGGCAGCTGGTGTGATCACATACATACTTCTCTGTGGATTCCCACCATTC CGAAGTGAGAACAATCTCCAGGAAGATCTCTTCGACCAGATCTTGGCTGGGAAGCTGGAG TTTCCGGCCCCCTACTGGGATAACATCACGGACTCTGCCAAGGAATTAATCAGTCAAATG CTTCAGGTAAATGTTGAAGCTCGGTGTACCGCGGGACAAATCCTGAGTCACCCCTGGGTG TCAGATGATGCCTCCCAGGAGAATAACATGCAAGCTGAGGTGACAGGTAAACTAAAACAG CACTTTAATAATGCGCTCCCCAAACAGAACAGCACTACCACCGGGGTCTCCGTCATCATG WO 00/73469 PCT/US00/14842

### FIGURE 2R

GTGAGTGGAAGGCGGCAGGTCTGGCCTGACTGCGGAGCCGGCCTTGAAGTTTTTGAATTA GGTAGCCGGGAGCTGCCCTCACATGGAAGTTGGTGCCTTCCGTAGTCCTATTTCATATGA AGATTGGCTTGGCATGTGGAGGGCACTCATTCGGCAACTCCCAGGCTTTGGGCACTGTGT GGAGGGGCTTGTGTAGGGACCAGCAGGCCTGGTGTGAGGGGTCCAGGCGTCAAGGAGCTC CTCCCAAGCCCTGGAGGGGTGTGTTGTGTTAGGAATTAACTCCCTGCCTACCCCAAGGCC TCAGAAATAGATTATTAGAGATGTGAATTATTCTTTGAGACTTGGGATAAGAAACAGCCA AAGCTAAACATATTTCAGTTTTTAAAAAATCAGTGTTTTATAAAACACAGTTTTGGGGCTTT TAAAGGTACATAATCAAGGAAAAAAATATATTCATTTTTCAGGGTTGGTAACATTTTA TGAGATGTCAGTGACAACGATGGCCTTATTTTTTTCAGCCTTTTCTTCTTCCAAAATGTT TCTTAAGGCAACTCTCCTAAATACATAAACACAACAAATTAAAATGAAAAGTGACATGAG AGTAAATGAATCAAAAGGAAAAAACATTGAACCAGAGGTGAGGGCAGCACCCCGCAGCA GCTGTCCAGGCCTGAGCCAATGCAACCCTGGGCGGGAAGGCCAGCTCACCGTGAGCAGGT AGAAGCCAGCCAGCCAGGCAGGGACCTTGGTTCTCCCCACACACTCCCAGGAGCAG GGAACAGGGGTGGAGTGGCCTTTCCCAGAGCTGGAGTTGGCTGCAGCAGCTTTCGAATCA GACCTGCCAAGGTGATGGGCGTCTGAGTTTCACATCTGGGCCCCCCGTGACCCCACTGAG TCCTGACAGCTAAGGATGGGCCACCTCCACAGCTCCGTCACTCGTACTTGGGACAGGCCT CTCATCCTCTGGGAAGGTCCTCCTTGTTTCCTACCCAACTAGAAGGGAAACAGTGGCATA GCTATAAGGAAGCCACACACATAACCCACATCCCCACACCCCCAACATCCCCCACACTCC CCACACCCCCACACCCCCACATCCCCACCATAATTACCCCCACCTCCAAATATCTCAT

SEO ID NO: 25 W30246 M SGK324 M ACCAAGTCCTCCAGCTCCTCCAACCAGCCCGGGAAGTTTCAGAGGATTGAAGATTTCT GCTCAGGGCAGATCTTCTTCCAACGTAAACGGTGGGCCTGAACTTGACCGTTGCCTGAGC  $\verb|CCTGAAGGTGTGAATGGAAACCGGTGCTCCGAGTCGTTCCCCCTTCTGGAGAAATACAGA| \\$ ATAGGGAAGGTCATCGGGGACGGCAACTTCGCGGTAGTTAAGGAGTGCGTGGACAGGTAC ACTGGAAAAGAGTTTGCATTAAAGATTATAGACAAAGCCAAATGCTGTGGAAAGGAGCAT CTGATTGAGAACGAAGTGTCAATCCTGCGCCGAGTGAAGCACCCCAACATCATCATGTTG GTTGAAGAGATGGAAACAGCAACTGACCTCTTTCTAGTGATGGAACTGGTCAAAGGTGGA GTGTACAACCTAGCCAATGCCCTCCGGTACCTGCACAGCCTCAGCATCGTCCACAGGGAC ATCAAGCCTGAGAATCTGCTGGTGTGCGAATACCCAGATGGAACCAAGTCTTTGAAGCTG GGAGACTTTGGGCTGGCGACGGTGGTTGAAGGCCCGTTGTACACGGTCTGTGGCACGCCA ACTTATGTGGCACCAGAGATCATAGCTGAAACAGGTTATGGCCTGAAGGTGGATGTTTGG GCAGCTGGTGTGATTACATACATACTTCTCTGTGGATTCCCACCATTCCGGAGTGAGAAC AATCTCCAGGAAGATCTCTTTGACCAGATCTTGGCTGGAAAGCTGGAATTCCCAGCCCCC TACTGGGACAACATTACAGACTCTCCTTGTGTGTGTTTTTAGGAAATGCTTATGAAGCTGG CCCGTGGGCTTCCCAGTGGGACGTGCAGCAGTTCTTGGCAGAGCAGGGCCAGCTCTGCTG TGTCATCTCCAGGGTCTCCCATCACCTCTGCTCTTTGCCATGGCAGGTCTGCTGAGACCC CGCGGGGACGGGGCATGGTGCTCCCTGATTGGCCTGTGACCAACCTTCTGGAAGGCTGC TGGCAGTTTTCCCTGTTTTCCACCACCCCACTCTTTTTAATAATTGTATATAACTGTACT TGTTCTACTTGCTTGTCTTTAAAACAGGGGCCCCCACAGTTCACTCTCACTGTTAGATTT TGCCTTTTCCAGGTATCCCCAACCTGCAATAAACTCTTCCCTCTTCAG

SEQ ID NO: 26\_AA383293\_H
CCAGCAGCCAAGAGGGTAGTGGTGTACCGGAATGGGGACCCATTCTTCCCAGGCTCCCAG
CTGGTGGTGACTCAACGCCGCTTCCCCACCATGGAGGCCTTCCTCTGCGAGGTGACATCA
GCTGTGCAGGCCCCACTGGCTGTGCGTGCCCTCTACACACCTTGTCATGGCCACCCTGTC
ACCAACCTGGCAGACTTGAAGAACAGAGGGCAGTATGTGGCCGCTGGATTTGAACGATTC

46/113

# FIGURE 2S

CACAAGCTCCCCCTTACCAGGCTTTTTGTCTCAGTGTGTTCAGGAATGGGGACCTGGTA AAGCTCCTGACTGAGAAGGTCAAGTTGCAGAGTGGGGCTGTGAGACTCTGCACCCTAGAG GGGCTCCCACTGTCAGCAGGGAAGGAGCTGGTAACTGGCCATTACTATGTGGCTGTCGGA GAGGATGAGTTCAAGGACCTTCCCTATCCAGCTCTGTCCACAAGAGGGGCTCCTGGCAGCA GGCAATGAAGCCCACCTGAGGAGTGGAGTGGGGACTGTCGCTGGTTCCCCCAAGCCTCTT GGAAGGAAGGCTAAGAAGGAGACATGCCTAATCGTGACCCTGACCCTGAAATACCAGCAG TCAGAAACAAGCAGAGACGGGCAATCATTCCCATCAGGAGTTATAGGAGTATATGGAGCT CCCCACCGAAGGAAGGAGACAGCGGGGGCCCTGGAAGTAGCAGATGATGAAGACACTCAG ACAGAGGAGCCCTTGGATCAGAGGGCAGCACAGATAGTGGAACAGGTTACTTGTCTGCAA GACTTTTTTGGTGATGACGATGTTTTTATTGCATGTGGACCAGAAAAATTTCGTTATGCC CAAGATGACTTTGTCCTGGATCATAGTCGTCGACGGCTCCTGAGAGAGCACCAGGCGGGC TTTGAGAAGCTCCGCAGGACCCGAGGAGAAGAAGGAGAAGAAGGAGAAAAAGCCA TGTATGTCTGGAGGCAGAAGGATGACTCTCAGAGATGACCAACCTGCAAAGCTAGAAAAG GAGCCCAAGACGAGGCCAGAAGAGAACAAGCCAGAGCGGCCCAGCGGTCGGAAGCCACGG CCCATGGGCATCATTGCCGCCAATGTGGAAAAGCATTATGAGACTGGCCGGGTCATTGGG ATGAAGATCATTGACAAGTCCAGACTCAAGGGCAAGGAGGACATGGTGGACAGTGAGATC TTGATCATCCAGAGCCTCTCTCACCCCAACATCGTGAAATTGCATGAAGTCTACGAAACA GACATGGAAATCTACCTGATCCTGGAGTACGTGCAGGGAGGAGACCTTTTTGACGCCATC ATAGAAAGTGTGAAGTTCCCGGAGCCCGATGCTGCCCTCATGATCATGGACTTATGCAAA GCCCTCGTCCACATGCACGACAAGAGCATTGTCCACCGGGACCTCAAGCCGGAAAACCTT TTGGTTCAGCGAAATGAGGACAAATCTACTACCTTGAAATTGGCTGATTTTGGACTTGCA AAGCATGTGGTGAGACCTATATTTACTGTGTGTGGGACCCCAACTTACGTAGCTCCCGAA ATTCTTTCTGAGAAAGGTTATGGACTGGAGGTGGACATGTGGGCTGCTGGCGTGATCCTC TATATCCTGCTGTGTGGCTTTCCCCCATTCCGCAGCCCTGAXXGAGGGGACCAGGACGAG CTCTTTAACATCATCCAGCTGGGCCACTTTGAGTTCCTCCCCCCTTACTGGGACAATATC TCTGATGCTGCTAAAGATCTGGTGAGCCGGTTGCTGGTGGTAGACCCCAAAAAGCGCTAC ACAGCTCATCAGGTTCTTCAGCACCCCTGGATCGAAACAGCTGGCAAGACCAATACAGTG AAACGACAGAAGCAGGTGTCCCCCAGCAGCGATGGTCACTTCCGGAGCCAGCACAAGAGG GTTGTGGAGCAGGTATCATAGTCACCACCTTGGGAATCTGTCCAGCCCCCAGTTCTGCTC AAGGACAGAGAAAAGGATAGAAGTTTGAGAGAAAAACAATGAAAGAGGCTTCTTCACATA ATTGGTGAATCAGAGGGAGAGACACTGAGTATATTTTAAAGCATATTAAAAAAATTAAGT CAATGTTAAATGTCACAACATATTTTTAGATTTGTATATTTAAAGCCTTTAATACATTTT TGGGGGGTAAGCATTGTCATCAGTGAGGAATTTTGGTAATAATGATGTGTTTTGCTTCCC CTTTGTAACCAAGTTTATTCTGTACTACAGGAGTGGTGCTTACCAGGGTCTAAACTCCCC CTGTGAGATTAATAAGGTGCATTG

# FIGURE 2T

AGTCACCGCTGTGGGGAGGCAGGAAGCTATAGCGCGGAAATGGAGAGTAAGGCAGTCTCT AGGCATCAGGGCAAGACTTCCACAGTGCTGGCCCCAGAAGACAAGGCGAGGGCCCAGAAG TGGGTAAGAGGGAAACAGGAGTCAGAACCTGGTGGCCCGCCTTCACCCGGGGCAGCCACT CAGGAGGAGACTCATGCAAGTGGAGAGAAACATCTGGGGGTGGAGATCGAAAAGACCTCC GGGGAGATTGTCAGATGTGAGAAGTGTAAGAGAGAAAGAGAGCTGCAGTTGGGCCTGCAG AGGGAGCCGTGCCCGCTGGGAACCAGTGAGCTGGACCTGGGGAGAGCTCAGAAGAGGGAT TCCGAGAAGTTGGTGAGGACCAAGAGCTGCAGGAGGCCTTCTAAGGCAAAATTTACAGAT GGAGAGGAAGGGTGAAGGCTGACAGCCATCGGGGCAGTCCCAGGGACCCCCCTCAGGAA ATGAGGAGGCCCAACAGCAACTCAGACAAGAAAGAGATCAGAGGCTCAGAAAGTCAGGAC AGTTATCCTCAGGGGGCACCCAAGGCCCAGAAGGACTTCGTGGAAGGGCCACCAGCTGTA GCCTGGCTCCGGAGAGAGCAGCAGGCCGAACCCCCACAGCTCCCCAGAACCCGAGGGGAG GAGAAGCAAGCAGAGCACGAGAAGAAGCCAGGCGGCTTAGGAGAGAGGAGGGCGCCAGAG AAGGAGTCTAAGAGGAAGCTAGAAGAGAGAGGCCAGAACGACCCAGTGGCCGGAAGCCG AGGCCCAAGGGCATCATCTCAGCGGATGTGGAGAAGCACTATGACATAGGTGGGGTCATT GGGGATGGCAACTTTGCCACCGTGAAGGAATGCAGGCACCGAGAGACCAAGCAGGCTTAC GCCATGAAGATGATTGACAAGTCCCAGCTGAAGGGTAAGGAGGACATTGTCGACAGTGAG ATTTTAATCATCCAGAGTCTCTCTCATCCCAACATTGTGAAACTGCATGAGGTCTACGAA ATCGTTGAAAATGTGAAGTTTCCAGAGCCCGAGGCTGCAGTTATGATCACAGACTTGTGT AAGGCCTTCGTCCACATGCACGACAAGAATATCGTCCACCGGGACGTGAAACCAGAAAAC GCCAAATATGTGGTGAGGCCTATATTTACTGTGTGTGGGACGCCAACATATGTAGCTCCT GAAATTCTTTCTGAGAAAGGTTACGGCCTGGAGGTGGACATGTGGGCGGCAGGTGTGATC CTATACATCCTCTTGTGTGGCTTCCCCCCTTTCCGAAGTCCTGAGAGGGACCAAGACGAG TCTGATGCTGCCAAAGATCTGGTGAGAAATTTGCTGGAGGTGGACCCTAAGAAGCGGTAC ACGGCCGAACAGGTCCTACAGCATCCCTGGATTGAGATGGTTGGGCATACCAACACAGGG AACTCACAGAAGGAGGAGTCCCCCAACAGTTTAGGTCACTTCCAGAGTCAGCACAAGAAG GTTGCAGAGCAGATGCCATAA

SEQ ID NO: 29 DRAK2\_H

CTCCGCTGCTGTCGCCAGGAGTCACTTCACGAGAAGCCAGGTCACAACCGTCGGCCCTTG TCTGGAAAAGTAAAAGTGGATCCTGCCACGTTCGGAGCTCCCTGGCGCCTCGCCCGGCTG GAGCTAGAGAACTCGTCCTGTGGCGGCCCCCGGCGTGGGGCGGGACAGCGGCCCCCTGGA GGGGCAGTCCCGGGAGAACCTGCGGCGGCCGGAGCGGTAAAAATAAGTGACTAAAGAAG CAGACCTGGGAATCACCTAACATGTCGAGGAGGAGATTTGATTGCCGAAGTATTTCAGGC CTACTAACTACAACTCCTCAAATTCCAATAAAAATGGAAAACTTTAATAATTTCTATATA CTTACATCTAAAGAGCTAGGGAGAGAAAATTTGCTGTGGTTAGACAATGTATATCAAAA CGGGCAGAAATTTTACACGAGATTGCTGTGCTTGAATTGGCAAAGTCTTGTCCCCGTGTT ATTAATCTTCATGAGGTCTATGAAAATACAAGTGAAATCATTTTGATATTGGAATATGCT GCAGGTGGAGAAATTTTCAGCCTGTGTTTACCTGAGTTGGCTGAAATGGTTTCTGAAAAT GATGTTATCAGACTCATTAAACAAATACTTGAAGGAGTTTATTATCTACATCAGAATAAC ATTGTACACCTTGATTTAAAGCCACAGAATATATTACTGAGCAGCATATACCCTCTCGGG GACATTAAAATAGTAGATTTTGGAATGTCTCGAAAAATAGGGCATGCGTGTGAACTTCGG GAAATCATGGGAACACCAGAATATTTAGCTCCAGAAATCCTGAACTATGATCCCATTACC ACAGCAACAGATATGTGGAATATTGGTATAATAGCATATATGTTGTTAACTCACACATCA CCATTTGTGGGAGAAGATAATCAAGAAACATACCTCAATATTTCTCAAGTTAATGTAGAT TATTCGGAAGAAACTTTTTCATCAGTTTCACAGCTGGCCACAGACTTTATTCAGAGCCTT

# FIGURE 2U

SEO ID NO: 30 W44160\_M DRAK2\_M CCAGACGCGGCTGCACTTTTCAAACCTCAACTGTAAGAAGCGTCGGTCAGCGTCTGTGCG GTCGCCGCCGGGAGTCGCCTCACAGGGGCCTGGCTGACGGCGACCAGCCGTTGTGGGGAA GAGTGCGAGGTAAAAGTCTGCCTAGAGAAGCAGGTCTGGCAGTCATCAACATGTCTCGGA GGAGATTCGATTGCCGAAGTGTCTCAGGCTTGCTAACTACAACCCCCTCAAACGCCGATTA AAACAGAGAATTTTAATAATTTCTATACTCTTACCCCAAAAGAACTTGGGAGAGGAAAAT TTGCTGTGGTTAGACAATGTATATCAAAATCAACTGGACAAGAGTATGCTGCCAAATCCC TGAAAAAGAGGAGAAGAGGCAGGATTGCCGGGCGGAAATTCTGCATGAGATAGCTGTGC TGGAGCTGGCCAGGTCTTGTCCCCACGTGATTAATCTGCATGAGGTCTACGAAAATGCAA CGGAAATCATTTTGGTGTTAGAATATGCTGCGGGTGGAGAAATTTTCAACCTGTGTTTAC CTGAGTTAGCCGAAATGGTATCTGAAAATGATGTTATCAGACTCATTAAACAAATCCTTG AAGGAGTTCATTATCTACATCAGAATAACATTGTTCACCTTGATTTAAAGCCACAGAATA TACTTTTGAGCAGTATATACCCACTCGGGGACATAAAAATTGTAGATTTTGGAATGTCTC GAAAAATTGGGAATGCAAGTGAGCTTCGGGAAATCATGGGAACACCTGAATACTTAGCTC CAGAAATCCTCAACTATGATCCCATTACCACAGCAACAGATATGTGGAATATTGGCATAA TAGCGTATATGTTGTTAACTCATACATCACCATTTGTAGGAGAAGATAATCAAGAAACAT ATCTGAATATTTCTCAAGTGAATGTAGATTATTCAGAAGAAATGTTTTCATCAGTTTCAC AGCTGGCCACAGACTTCATCCAGAGCCTTCTAGTAAAGAACCCAGAGAAAAGACCAACAG CAGAATCCTGCCTATCCCACTCATGGCTGCAGCAGTGGGACTTTGGAAGCTTGTTTCATC CTGAGGAAACTTCAGGCTCCTCTCAAATTCAGGATCTGACTCTCAGGTCCTCTGAAGAGA AGACCTCCAAGTCCTCCTGTAATGGGAGCTGTGGAGCCCGGGAGGACAAGGAGAACATCC CTGAAGATGGCAGCTTAGTTTCTAAAAGATTTCGATTCGATGACTCCTTGCCCAGCCCCC CGGAAATTTGAAATCTCTGGTGTGAGATTGTGTTTGTAGCTTCATATATTATGTTTATAT TATAAATGCACTTCTGCTTAGAAGAACTTAAGGAACAGTTTAAATGCTAGGCTTCTGTTG GCTAGCATATCATTTCTTGTCCTGAAATTGTTTTGCAGAGGAAAATATTTAAGTATATGA CAAAAAATGTAAATTGTGTTTAAGAGAACACATGCAACTGAAAGAACTCAAGTTCAGTCA TTAGTAGGTTCTAAGGTAAGCCCTATACCATAACTCTATTACAGAGAATCTGTTTGGGGA TAGTTGAAAGTATTTCCCAGTTACCAATAATAGCTTGAAACTGTAAGATTTTCTTTGTGT GCCATGTGCTCGGTGAGAGGACACAGTCAACCAGAGCAGGGTTGATCCAGGCTGTTTCTC TGCAAACCGAGTCAAAACTCGACATCATTTCCAGCTCATGTATTTTGTACGTGCATCATA TATCAGATCTAATAAGATCTGGAAGATGGATATGCAAATAAGAGGCCTTTGTCTTAGA TTCATAAAGGGAAATGTTAAGTTCTGGCAGCTGACTTAGTGTTGGATGTCTCCTAAGTCT CAGGATAGAAGCCCATCATTAGAGCATAGGCACTTCAGGAATTCTTGTGTGAAATTCTAG CACAACACATGGGAGTGTTCAGTGTTGTCCGTGGTCAATATCTATGTTCAGTCCTGATGG

### FIGURE 2V

GAGGGGCCTAGGGACTGCTTTGGAGATTTCCCACTGGTGTCCATTTTAAGGTCTGTAATA
ATGTCATGTTAAGATAACAGATCTCATAAATATGCTACTCTATCAGACTCCGTTGCCAAA
ACAAATTAAAAGCCTGTGTATTGAAGTGGGTGTTAGTCTAACAACCTGTAAATTCTTGAA
ATTGTTACTAAAATTCCAAATTCTTTAGATAACTTTAAACTATTTAAATTGAGCATTGCT
GTCTTTGTTTGATTAAAGGTTGAGTTCCTTTATATCTGTTATTTTTAAAGGAAAAGTTGT
TTGCCTTTTGTATATGTGTGTGCATATGTGTATGTGTACAGGTATATGTATATGTATT
GATAGATAAAATACAGCCTTTAAACAACTTC

SEO ID NO: 31 H01248 H, DRAK1\_H ATGATCCCTTTGGAGAAGCCAGGCAGCGGCGCCTCCTCCCCAGGCGCCACCTCAGGCTCG GGCCGGGCAGGCCGGGGTCTGAGCGGGCCGTGCCGGCCGCCGCCGCCCCAGGCCCGC GGGCTGCTGACAGAGATACGCGCCGTGGTGCGCACCGAGCCCTTCCAGGACGGCTACAGC CTGTGCCCGGGCCGGGAGCTGGGCAGGGGGAAATTTGCAGTGGTGAGAAAATGTATAAAG AAAGATTCTGGGAAAGAATTTGCTGCAAAGTTCATGAGAAAAAGAAGAAAAAGGCCAAGAT TGTCGGATGGAAATAATTCATGAGATTGCTGTACTTGAACTAGCACAAGACAATCCTTGG GTCATTAATTTACATGAAGTTTATGAGACTGCATCAGAAATGATCTTAGTTCTGGAATAT AAAGATGTTCAAAGACTTATGCGACAGATTTTAGAAGGTGTTCACTTTTTACACACTCGT GATGTAGTTCATCTTGATTTGAAGCCTCAGAATATTCTGTTGACAAGTGAATCTCCATTG GGTGACATTAAGATTGTTGATTTTGGCCTTTCAAGAATATTGAAGAACAGTGAAGAGCTC CGAGAAATTATGGGTACCCCTGAATATGTGGCTCCTGAAATTCTTAGTTATGATCCTATA AGCATGGCAACAGATATGTGGAGCATTGGAGTGTTAACATATGTCATGCTTACAGGAATA TCACCTTTCTTAGGCAATGATAAACAAGAAACATTCTTAAACATCTCACAGATGAATTTA AGTTATTCTGAGGAAGAATTTGATGTTTTGTCTGAGTCGGCTGTTGATTTCATCAGGACA CTTTTAGTTAAGAAACCTGAAGATCGAGCCACTGCTGAAGAATGTCTAAAGCACCCCTGG TTGACACAGAGCAGTATTCAAGAGCCTTCTTTCAGGATGGAAAAGGCACTAGAAGAAGCA ACCGAGGAATCCATTGTAACCGAAGAGTTAATTGTAGTTACTTCATATACTCTAGGACAA TGCAGACAGTCTGAAAAAGAGAAAATGGAGCAAAAGGCCATTTCCAAACGATTTAAATTT GAGGAACCTTTGCTACAAGAAATTCCAGGAGAATTTATCTACTGA

SEO ID NO: 32 AA021445 H CCCAGCCCGGCCTCCCGCGGACCCATGCCCGCCCGTATCGGCTACTACGAGATCGACCG CACCATCGGCAAGGGCAACTTCGCGGTGGTCAAGCGGGCCACGCACCTCGTCACCAAGGC CAAGGTTGCTATCAAGATCATAGATAAGACCCAGCTGGATGAAGAAAACTTGAAGAAGAT TTTCCGGGAAGTTCAAATTATGAAGATGCTTTGCCACCCCCATATCATCAGGCTCTACCA GGTTATGGAGACAGAACGGATGATTTATCTGGTGACAGAATATGCTAGTGGAGGGGAAAT ATTTGACCACCTGGTGGCCCATGGTAGAATGGCAGAAAAGGAGGCACGTCGGAAGTTCAA ACAGATCGTCACAGCTGTCTATTTTTGTCACTGTCGGAACATTGTTCATCGTGATTTAAA AGCTGAAAATTTACTTCTGGATGCCAATCTGAATATCAAAATAGCAGATTTTGGTTTCAG ACCTGAACTCTTTGAAGGAAAAGAATATGATGGGCCCAAAGTGGACATCTGGAGCCTTGG AGTTGTCCTCTACGTGCTTGTGTGCGGTGCCCTGCCATTTGATGGAAGCACACTGCAGAA TCTGCGGGCCCGCGTGCTGAGTGGAAAGTTCCGCATCCCATTTTTTATGTCCACAGAATG TGAGCATTTGATCCGCCATATGTTGGTGTTAGATCCCAATAAGCGCCTCTCCATGGAGCA GATCTGCAAGCACAAGTGGATGAAGCTAGGGGACGCCGATCCCAACTTTGACAGGTTAAT AGCTGAATGCCAACAACTAAAGGAAGAAAGACAGGTGGACCCCCTGAATGAGGATGTCCT CTTGGCCATGGAGGACATGGGACTGGACAAAGAACAGACACTGCAGTCATTAAGATCAGA

# FIGURE 2W

TGCCTATGATCACTATAGTGCAATCTACAGCCTGCTGTGTGATCGACATAAGAGACATAA AACCCTGCGTCTCGGAGCACTTCCTAGCATGCCCCGAGCCCTGGCCTTTCAAGCACCAGT CAATATCCAGGCGGAGCAGGCAGGTACTGCTATGAACATCAGCGTTCCCCAGGTGCAGCT GATCAACCCAGAGAACCAAATTGTGGAGCCGGATGGGACACTGAATTTGGACAGTGATGA GGGTGAAGAGCCTTCCCCTGAAGCATTGGTGCGCTATTTGTCAATGAGGAGGCACACAGT GGGTGTGGCTGACCCACGCACGGAAGTTATGGAAGATCTGCAGAAGCTCCTACCTGGCTT TCCTGGAGTCAACCCCCAGGCTCCATTCCTGCAGGTGGCCCCTAATGTGAACTTCATGCA CAACCTGTTGCCTATGCAAACTTGCAACCAACCGGGCAACTTGAGTACAAGGAGCAGTC TCTCCTACAGCCGCCCACGCTACAGCTGTTGAATGGAATGGGCCCCCTTGGCCGGAGGGC ATCAGATGGAGGAGCCAACATCCAACTGCATGCCCAGCAGCTGCTGAAGCGCCCACGGGG ACCCTCTCCGCTTGTCACCATGACACCAGCAGTGCCAGCAGTTACCCCTGTGGACGAGGA GAGCTCAGACGGGGAGCCAGACCAGGAAGCTGTGCAGAGGTACTTGGCAAATAGGTCCAA AAGACATACACTGGCCATGACCAACCCTACAGCTGAGATCCCACCGGACCTACAACGGCA GCTAGGACAGCCTTTCCGTTCCCGGGTCTGGCCTCCTCACCTGGTACCTGATCAGCA TCGCTCTACCTACAAGGACTCCAACACTCTGCACCTCCCTACGGAGCGTTTCTCCCCTGT GCGCCGGTTCTCAGATGGGGCTGCGAGCATCCAGGCCTTCAAAGCTCACCTGGAAAAAAT GGGCAACAACAGCAGCATCAAACAGCTGCAGCAGGAGTGTGAGCAGCTGCAGAAGATGTA CGGGGGGCAGATTGATGAAAGAACCCTGGAGAAGACCCAGCAGCAGCATATGTTATACCA GCAGGAGCAGCATCAAATTCTCCAGCAACAAATTCAAGACTCTATCTGTCCTCCA CCAGAGGTTAAGGATTCAGCCTTCAAGCCCACCCCCAACCACCCCCAACAACCATCTCTT CAGGCAGCCCAGTAATAGTCCTCCCCCCATGAGCAGTGCCATGATCCAGCCTCACGGGGC TGCATCTTCTCCCAGTTTCAAGGCTTACCTTCCCGCAGTGCAATCTTTCAGCAGCAACC TGAGAACTGTTCCTCCCCCAACGTGGCACTAACCTGCTTGGGTATGCAGCAGCCTGC TCAGTCACAGCAGGTCACCATCCAAGTCCAAGAGCCTGTTGACATGCTCAGCAACATGCC AGGCACAGCTGCAGGCTCCAGTGGGCGCGCATCTCCATCAGCCCCAGTGCTGGTCAGAT GCAGATGCAGCACCGTACCAACCTGATGGCCACCCTCAGCTATGGGCACCGTCCCTTGTC CAAGCAGCTGAGTGCTGACAGTGCAGAGGCTCACAGCTTGAACGTGAATCGGTTCTCCCC TGCTAACTACGACCAGGCGCATTTACACCCCCATCTGTTTTCGGACCAGTCCCGGGGTTC CCCCAGCAGCTACAGCCCTTCAACAGGAGTGGGGTTCTCTCCAACCCAAGCCCTGAAAGT CCCTCCACTTGACCAATTCCCCACCTTCCCTCCCAGTGCACATCAGCAGCCGCCACACTA TACCACGTCGGCACTACAGCAGGCCCTGCTGTCTCCCACGCCGCCAGACTATACAAGACA CCAGCAGGTACCCCACATCCTTCAAGGACTGCTTTCTCCCCGGCATTCGCTCACCGGCCA CTCGGACATCCGGCTGCCCCCAACAGAGTTTGCACAGCTCATTAAAAGGCAGCAGCAACA ACGGCAGCAGCAGCAGCAGCAACAGCAAGAATACCAGGAACTGTTCAGGCACAT GAACCAAGGGGATGCGGGGAGTCTGGCTCCCAGCCTTGGGGGACAGAGCATGACAGAGCG CCAGGCTTTATCTTATCAAAATGCTGACTCTTATCACCATCACACCAGCCCCCAGCATCT GTATGCTCACCAGCCGGCACTGATGCATTCAGAGAGCATGGAGGAGGACTGCTCGTGTGA GGGGGCCAAGGATGGCTTCCAAGACAGTAAGAGTTCAAGTACATTGACCAAAGGTTGCCA TGACAGCCCTCTGCTCTTGAGTACCGGTGGACCTGGGGACCCTGAATCTTTGCTAGGAAC TGTGAGTCATGCCCAAGAATTGGGGATACATCCCTATGGTCATCAGCCAACTGCTGCATT CAGTAAAAATAAGGTGCCCAGCAGAGAGCCTGTCATAGGGAACTGCATGGATAGAAGTTC TCCAGGACAAGCAGTGGAGCTGCCGGATCACAATGGGCTCGGGTACCCAGCACGCCCCTC CGTCCATGAGCACCACAGGCCCCGGGCCCTCCAGAGACACCACACGATCCAGAACAGCGA CGATGCTTATGTACAGCTGGATAACTTGCCAGGAATGAGTCTCGTGGCTGGGAAAGCACT GTTTCAGGATGGGGAAAATGAGGAATGTGGGGCAAGCCTGGGAGGTCATGAGCACCCAGA CCTGAGTGATGGCAGCCAGCATTTAAACTCCTCTTGCTATCCATCTACGTGTATTACAGA  WO 00/73469 PCT/US00/14842 .

### FIGURE 2X

SEQ ID NO: 33\_2R22-5-11 H CTGGGCCGCTGCCGGTCAGGTCGGCCCCCTGACAGCTCCGGGAGCCTCAAGCGCGACA GGGCGCCTCACCTCGGGACATCCACACCCGACCGCTCCTGCTCCAGAGGCAACAACCC AGCGCGCCTAGCCTGGCGCGTGCAGCGAAGCCCAAGAGCTGGCCTCGCCACGAAGGTTG GGCTAAAGTGACATTGCAGGGATTAAATCCTTCTTTGGCTGCCTGTGTGACCAGAAGGCT TATTTGCAAGTTTCTTCTTTCCTGGGGTCCAGATTATTAGGTCTCCAGCGCCCTGCAGCT GGCCTCCCAGGGGCATTTACGCACCAGAGTGCAAGATTCTCTGGCCATCAAGGGAAATAG CAAACAGAAGCCTTTGTCCTGGGGCACAGCCACCTACCACAAAGCATCAGACTCCACGTC TGGCCAGAAAGTTCCTGGAGTCCCATCAGGCCAGTGGGTATGTAACATGTGCCTAATTGT CAGCTCCTGGCTGGGCAGACTCAGCTACCACGTTCACTGCCTTCCTCTCACTAAA GCCGAGAGGGAGGCTGCTCAGCTCTCAGGAAAACTCTTTTGAACCCTGGGCACCTGCTGT CCTCAGTTGGCATCTCCCACCCTCTGAGCCTCTTCTGCTCCTGCACAACCTGCCTCTTCG CTGAGATGGAGACGTGAGCCCCGTGGACGATGACTGCAGTGTATATGAATGGAGGTGGC CTGGTGAACCCCCACTATGCCCGGTGGGATCGGCGCGACAGTGTAGAAAGTGGCTGTCAG ACCGAGAGTAGCAAGGAGGTGAGGAGGGGACAGCCCCGCCAGCTGACGCCCTTCGAGAAA CTGACACAGGACATGTCCCAGGATGAGAAGGTGGTGAGGGAGATCACGCTGGGGAAACGG ATAGGCTTCTACCGAATTCGAGGGGAAATCGGAAGTGGAAACTTCTCCCAAGTGAAGCTT GGGATTCACTCCCTAACCAAAGAAAAGGTGGCCATTAAGATCCTGGACAAGACCAAGTTA GACCAGAAAACCCAGAGGCTACTATCCCGAGAAATCTCCAGCATGGAAAAGCTGCACCAT CCCAACATCATCCGCCTTTACGAAGTGGTGGAGACCCTATCCAAGCTGCACTTGGTGATG GAGTATGCAGGGGGTGGGGAGCTCTTCGGAAAAATTAGCACTGAGGGGAAGCTCTCTGAA CAAATTATTCATAGAGATCTGAAAGCAGAAAATGTATTCTATACCAGTAATACTTGTGTG AAGGTGGGCGATTTTGGATTCAGCACAGTAAGCAAAAAAGGTGAAATGCTGAACACTTTC TGTGGGTCTCCTCCCTACGCTGCGCCTGAACTCTTCCGGGACGAGCACTACATCGGCATT TACGTGGATATCTGGGCCTTGGGGGTGCTTTTGTACTTCATGGTGACTGGCACCATGCCA TTTCGGGCAGAACCGTGGCCAAACTAAAAAAGAGCATCCTCGAGGGCACATACAGTGTA CCGCCGCACGTGTCAGAGCCCTGCCACCGACTCATCCGAGGAGTCCTTCAGCAGATCCCC CCTACACCTTTGGAACCTTTCCAACTGGATCCCAAACATTTGTCGGAAACCAGCACTCTC AAGGAAGAAAATGAGGTCAAAAGCACTTTAGAACATTTGGGCATTACAGAAGAGCAT ATTCGAAATAACCAAGGGAGAGATGCTCGCAGCTCAATCACAGGGGTCTATAGAATTATT TTACATAGAGTCCAAAGGAAGAAGGCTTTGGAAAGTGTCCCAGTCATGATGCTACCAGAC CCTAAAGAAGAGACCTCAAAAAAGGGTCCCGTGTCTACAGAGGGATAAGACACACATCC GCTGCTTCTAAATTTTTTCAAGGACAACTTGAGTGGAGACATTTTTGTAATTTTTAAAT AAACTTAAATTTGAGATATGCAAAAAAAAAA

SEQ ID NO: 34\_R31237\_1\_H, AAC33487
ATGTCCACTAGGACCCCATTGCCAACGGTGAATGAACGAGACACTGAAAACCACACGTCA
CATGGAGATGGGCGTCAAGAAGTTACCTCTCGTACCAGCCGCTCAGGAGCTCGGTGTAGA

52/119

#### FIGURE 2Y

AACTCTATAGCCTCCTGTGCAGATGAACAACCTCACATCGGAAACTACAGACTGTTGAAA ACAATCGGCAAGGGGAATTTTGCAAAAGTAAAATTGGCAAGACATATCCTTACAGGCAGA GAGGTTGCAATAAAAATAATTGACAAAACTCAGTTGAATCCAACAAGTCTACAAAAGCTC TTCAGAGAAGTAAGAATAATGAAGATTTTAAATCATCCCAATATAGTGAAGTTATTCGAA GTCATTGAAACTGAAAAAACACTCTACCTAATCATGGAATATGCAAGTGGAGGTGAAGTA TTTGACTATTTGGTTGCACATGGCAGGATGAAGGAAAAAGAAGCAAGATCTAAATTTAGA CAGATTGTGTCTGCAGTTCAATACTGCCATCAGAAACGGATCGTACATCGAGACCTCAAG GCTGAAAATCTATTGTTAGATGCCGATATGAACATTAAAATAGCAGATTTCGGTTTTAGC AATGAATTTACTGTTGGCGGTAAACTCGACACGTTTTGTGGCAGTCCTCCATACGCAGCA CCTGAGCTCTTCCAGGGCAAGAAATATGACGGGCCAGAAGTGGATGTGTGGAGTCTGGGG GTCATTTTATACACACTAGTCAGTGGCTCACTTCCCTTTGATGGGCAAAACCTAAAGGAA CTGAGAGAGAGTATTAAGAGGGAAATACAGAATTCCCTTCTACATGTCTACAGACTGT GAAAACCTTCTCAAACGTTTCCTGGTGCTAAATCCAATTAAACGCGGCACTCTAGAGCAA ATCATGAAGGACAGGTGGATCAATGCAGGGCATGAAGAAGATGAACTCAAACCATTTGTT GAACCAGAGCTAGACATCTCAGACCAAAAAAGAATAGATATTATGGTGGGAATGGGATAT TCACAAGAAGAAATTCAAGAATCTCTTAGTAAGATGAAATACGATGAAATCACAGCTACA TATTTGTTATTGGGGAGAAAATCTTCAGAGCTGGATGCTAGTGATTCCAGTTCTAGCAGC AATCTTTCACTTGCTAAGGTTAGGCCGAGCAGTGATCTCAACAACAGTACTGGCCAGTCT CCTCACCACAAAGTGCAGAGAAGTGTTTCTTCAAGCCAAAAGCAAAGACGCTACAGTGAC CATGCTGGACCAGCTATTCCTTCTGTTGTGGCGTATCCGAAAAGGAGTCAGACAAGCACT GCAGATGGTGACCTCAAAGAAGATGGAATTTCCTCCCGGAAATCAAGTGGCAGTGCTGTT GGAGGAAAGGGAATTGCTCCAGCCAGTCCCATGCTTGGGAATGCAAGTAATCCTAATAAG GCGGATATTCCTGAACGCAAGAAAAGCTCCACTGTCCCTAGTAGTAACACAGCATCTGGT GGAATGACACGACGAAATACTTATGTTTGCAGTGAGAGAACTACAGCTGATAGACACTCA GTGATTCAGAATGGCAAAGAAAACAGCACTATTCCTGATCAGAGAACTCCAGTTGCTTCA ACACACAGTATCAGTAGTGCAGCCACCCCAGATCGAATCCGCTTCCCAAGAGGCACTGCC AGTCGTAGCACTTTCCACGGCCAGCCCCGGGAACGGCGAACCACATATAATGGCCCT CCTGCCTCTCCCAGCCTGTCCCATGAAGCCACACCATTGTCCCAGACTCGAAGCCGAGGC TCCACTAATCTCTTTAGTAAATTAACTTCAAAACTCACAAGGAGTCGCAATGTATCTGCT GAGCAAAAAGATGAAAACAAAGAAGCAAAGCCTCGATCCCTACGCTTCACCTGGAGCATG AAAACCACTAGTTCAATGGATCCCGGGGACATGATGCGGGAAATCCGCAAAGTGTTGGAC GCCAATAACTGCGACTATGAGCAGAGGGAGCGCTTCTTGCTCTTCTGCGTCCACGGAGAT GGGCACGCGGAGAACCTCGTGCAGTGGGAAATGGAAGTGTGCAAGCTGCCAAGACTGTCT CTGAACGGGGTCCGGTTTAAGCGGATATCGGGGACATCCATAGCCTTCAAAAATATTGCT TCCAAAATTGCCAATGAGCTAAAGCTGTAA

SEQ ID NO: 35\_W90839\_M

AAAGGGCCGTCCTGGTCCAGCCGTTCCCTGGGTGCCCGTTGCCGGAACTCTATCGCTTCC
TGCCCTGAGGAACAACCCCATGTGGGCAACTATAGGCTGCTAAGGACCATCGGGAAGGGC
AACTTCGCCAAAGTCAAGCTGGCTCGGCATATCCTCACGGGCCGGGAGGTCGCTATTAAG
ATCATTGATAAGACCCAGCTGAACCCCAGTAGCTTGCAGAAGCTGTTCAGAGAAGTCCGA
ATTATGAAGGGACTCAACCACCCCAACATCGTGAAGCTTTTTGAGGTGATAGAGACGGAG
AAGACGCTATACCTGGTGATGGAATACGCTAGCGCAGGAGAAGTGTTTGACTACCTCGTG
TCGCACGGCCGCATGAAGGAGAAGAACATTGTACACAGGGATCTAAAAGGCTGAAAACCTGTTG
CTGGATGCCGAGGCCAACATCAAAATCGCCGACTTCGGCTTCAGCAATGAGTTCACGCTG
GGCTCCAAGCTGGACACCTTCTGTGGGAGCCCCCCATACGCCGCCCCAGAGCTGTTCCAG
GGCAAGAAGTATGATGGGCCAGAGGTGGACATCTGAGCCTGGTTCACACG
CTGGTCAGCGGCTCCCTGCCCTTCGATGGGCACACCTCAAGGAGCTGCCGGAGCCAGTC
CTCGTCAGCGGGTCCCTTCCGATGGGCACACCTCAAGGAGCTGCGGGAGCCAGTC
CTCAGAGGAAAGTACCGGGTCCCCTTCTACATGTCTACAGACTGCGAGAGCATTCTGCGG

# FIGURE 2Z

SEQ ID NO: 36\_406786.5 H GTAGCCGGCTTGGCGTGACCGTCGCCTGATCCAGTTGTTAGAGGTGGAAGCTTGGCAGTT GGCCTCCCTTCTTCCCATGGAGGTCGGGGGCTTAACAGTCTTTGAAGAGGACCAGAGATG CCTTTCCCAGAGCCTCCCCTTGCCAGTGTCAGCAGAGGGCCCAGCTGCACAGACCACTGC TGAGCCCAGCAGGTCGTTTTCCTCAGCCCACAGACACCTGAGCAGAAGGAATGGGCTTTC CAGACTCTGCCAGAGCAGGACGGCGCTCTCTGAAGACAGATGGAGCTCCTATTGTCTATC ATCACTGGCTGCCCAGAATATTTGTACAAGTAAACTGCACTGCCCTGCTGCCCCTGAGCA CACGGACCCGTCCGAACCGCGGGGCAGTGTGTCCTGCTGCTGCTGCTGCGGGGACTGTC CTCAGGGTGGTCCTCACCTCTGCTTCCGGCCCCTGTGTGCAACCCTAACAAGGCCATCTT CACGGTGGATGCCAAGACCACAGAGATCCTCGTTGCTAACGACAAAGCTTGCGGGCTCCT TTCTGATGTGGTGGAGGCCCTCAGCGAGGAGCACATGGAGGCCGACGCCACGCTGCGGT GGTGTTTGGCACGGTGGTGGACATCATCACCCGTAGTGGGGAGAAGATTCCAGTGTCTGT GTGGATGAAGAGGATGCGGCAGGAGCGCCCCTATGCTGCGTGGTGGTCCTGGAGCCCGT GGAGAGGGTCTCGACCTGGGTCGCTTTCCAGAGCGATGGCACCATCACGTCATGTGACAG TCTCTTTGCTCATCTTCACGGGTACGTGTCTGGGGAGGACGTGGCTGGGCAGCATATCAC AGACCTGATCCCTTCTGTGCAGCTCCCTCCTTCTGGCCAGCACATCCCAAAGAATCTCAA GATTCAGAGGTCTGTTGGAAGAGCCAGGGACGGTACCACCTTCCCTCTGAGCTTAAAGCT GAAATCCCAACCCAGCAGCGAGGAGGCGACCACCGGTGAGGCGGCCCCTGTGAGCGGCTA CCGGGCATCTGTCTGGGTGTTCTGCACCATCAGTGGCCTCATCACCCTCCTGCCGGATGG GACCATCCACGGCATCAACCACAGCTTCGCGCTGACACTGTTTGGTTACGGAAAGACGGA GCTCCTGGGCAAGAATATCACTTTCCTGATTCCTGGTTTCTACAGCTACATGGACCTTGC GTACAACAGCTCATTACAGCTCCCAGACCTGGCCAGCTGCCTGGACGTCGGCAATGAGAG TGGGTGTGGGGAGAGACCTTGGACCCGTGGCAGGCCCAGGACCCAGCTGAGGGGGCCCA GGATCCAAGGATTAATGTCGTGCTTGCTGGTGGCCACGTTGTGCCCCGAGATGAGATCCG GAAGCTGATGGAAAGCCAAGACATCTTCACCGGGACTCAGACTGAGCTGATTGCTGGAGG CCAGCTCCTTTCCTGCCTCTCACCTCAGCCTGCTCCAGGGGTGGACAATGTCCCAGAAGG AAGCCTGCCAGTGCACGGTGAACAGGCGCTGCCCAAGGACCAGCAAATCACTGCCTTGGG GAGAGAGGAACCTGTGGCAATAGAGAGCCCCGGACAGGATCTTCTGGGAGAAAGCAGGTC TGAACCAGTGGATGTGAAGCCATTTGCTTCCTGCGAAGATTCTGAAGCTCCAGTCCCAGC TGAGGATGGGGGCAGTGATGCTGGCATGTGTGGCCTGTGTCAGAAGGCCCAGCTAGAGCG GATGGGAGTCAGTGGTCCCAGCGGTTCAGACCTTTGGGCTGGGGCTGCCGTGGCCAAGCC CCAGGCCAAGGGTCAGCTGGCGGGGGGCAGCCTCCTGATGCACTGCCCTTGCTATGGGAG TGAATGGGGCTTGTGGTGGCGAAGCCAGGACTTGGCCCCCAGCCCCTCTGGGATGGCAGG CCTCTCGTTTGGGACACCTACTCTAGATGAGCCGTGGCTGGGAGTGGAAAACGACCGAGA

### **FIGURE 2AA**

AGAGCTGCAGACCTGCTTGATTAAGGAGCAGCTGTCCCAGTTGAGCCTTGCAGGAGCCCT GGATGTCCCCCACGCCGAACTCGTTCCGACAGAGTGCCAGGCTGTCACCGCTCCTGTGTC GTCCTGCGATCTGGGAGGCAGAGACCTGTGCGGTGGCTGCACGGGCAGCTCCTCAGCCTG CTATGCCTTGGCCACGGACCTCCCTGGGGGCCTGGAAGCAGTGGAGGCCCAGGAGGTTGA GTCATCAAATTGTTCCTGTGCTACGTCTGAACTCAGAGAGACACCCTCTTCCTTGGCAGT GGGCTCCGATCCAGATGTAGGCAGTCTCCAGGAACAGGGGTCGTGTGTCCTGGATGACAG GGAGCTGTTACTACTGACCGGCACCTGTGTTGACCTTGGCCAAGGCCGACGGTTCCGGGA TGAGGACACGTGCCCATCAGCAGAGGAGCCAAGGCTGAACGTCCAGGTCACCTCCACGCC CGTGATCGTGATGCGCGGGGCTGCTGGCCTGCAGCGGGAGATCCAGGAGGGTGCCTACTC CGGGAGCTGCTACCATCGAGATGGCTTACGGCTGAGTATACAGTTTGAGGTGAGGCGGGT CCAACGCGACTCAGCCGCCAGGACCCGCCTGTTCCTTGCCAGCCTGCCCGGCTCCACCCA CTCTACCGCTGCTGAGCTCACCGGACCCAGCCTGGTGGAAGTGCTCAGAGCCAGACCCTG GTTTGAGGAGCCCCCAAGGCTGTGGAACTGGAGGGGTTGGCGGCCTGTGAGGGCGAGTA CTCCCAAAAGTACAGTACCATGAGCCCGCTGGGCAGTGGGGCCTTCGGCTTCGTGTGGAC TGCTGTGGACAAGGAAAAAACAAGGAGGTGGTGGAAGTTTATTAAGAAGGAGAAGGT CTTGGAGGATTGTTGGATTGAGGATCCCAAACTTGGGAAAGTTACTTTAGAGATCGCAAT TCTATCCAGGGTGGAGCACGCCAATATCATCAAGGTATTGGATATATTTGAAAACCAAGG GTTCTTCCAGCTTGTGATGGAGAAGCACGGCTCCGGCCTAGACCTCTTCGCTTTCATCGA CCGCCACCCCAGGCTGGATGAGCCCCTGGCGAGCTACATCTTCCGACAAGTGAGAGCAGG CCAGAGCCGTCTAGTGTCAGCAGTGGGATACCTGCGCTTGAAGGACATCATCCACCGTGA CATCAAGGATGAGAACATCGTGATCGCTGAGGACTTCACAATCAAGCTGATAGACTTTGG CTCGGCCGCCTACTTGGAAAGGGGAAAATTATTTTATACTTTTTGTGGGACCATCGAGTA CTGTGCACCGGAAGTTCTCATGGGGAATCCCTACAGAGGGCCGGAGCTGGAGATGTGGTC TCTGGGAGTCACTCTGTACACGCTGGTCTTTGAGGAGAACCCCTTCTGTGAGCTGGAGGA GACCGTGGAGGCTGCCATACACCCGCCATACCTGGTGTCCAAAGAACTCATGAGCCTTGT GTCTGGGCTGCTGCAGCCAGTCCCTGAGAGACGCACCACCTTGGAGAAGCTGGTGACAGA CCCGTGGGTAACACAGCCTGTGAATCTTGCTGACTATACATGGGAAGAGGTGTTTCGAGT AAACAAGCCAGAAAGTGGAGTTCTGTCCGCTGCGAGCCTGGAGATGGGGAACAGGAGCCT GAGTGATGTGGCCCAGGCTCAGGAGCTTTGTGGGGGCCCCGTTCCAGGCGAGGCTCCTAA TGGCCAAGGCTGTTTGCATCCCGGGGATCCCCGTCTGCTGACCAGCTAAACACCAATTTC TTCCTGCTTTTCTCCACTTGGTTTGGAAAATCACACAGTTTTCAGGCTCCATCTGTTTG

### FIGURE 2BB

SEO ID NO: 38 AA785735 H GGCACGAGGCGCCTGGGCTGGGCCCTGCGGAGGANGGGAAGGAGCGAAGGAGCGAAGGA CTCCTGTCCGCCGTGTCTAGCAGCGGGGCCCAGCATGGTCATGGCGGATGGCCCGAGGCA CTTGCAGCGCGGGCCGGTCCGGGTGGGGTTCTACGACATCGAGGGCACGCTGGGCAAGGG CAACTTCGCTGTGGTGAAGCTGGGGCGGCACCGGATCACCAAGACGGAGGTGGCAATAAA AATAATCGATAAGTCTCAGCTGGATGCAGTGAACCTTGAGAAAATCTACCGAGAAGTACA AATAATGAAAATGTTAGACCACCCTCACATAATCAAACTTTATCAGGTAATGGAGACCAA AAGTATGTTGTACCTTGTGACAGAATATGCCAAAAATGGAGAAATTTTTTGACTATCTTGC TAATCATGGCCGGTTAAATGAGTCTGAAGCCAGGCGAAAATTCTGGCAAATCCTGTCTGC TGTTGATTATTGTCATGGTCGGAAGATTGTGCACCGTGACCTCAAAGCTGAAAATCTCCT GCTGGATAACAACATGAATATCAAAATAGCAGATTTCGGTTTTGGAAATTTCTTTAAAAG TGGTGAACTGCTGGCAACATGGTGTGGCAGCCCCCCTTATGCAGCCCCAGAAGTCTTTGA AGGGCAGCAGTATGAAGGACCACAGCTGGACATCTGGAGTATGGGAGTTGTTCTTTATGT CCTTGTCTGTGGAGCTCTGCCCTTTGATGGACCGACTCTTCCAATTTTGAGGCAGAGGGT TCTGGAAGGAAGATTCCGGATTCCGTATTTCATGTCAGAAGATTGCGAGCACCTTATCCG AAGGATGTTGGTCCTAGACCCATCCAAACGGCTAACCATAGCCCAAATCAAGGAGCATAA ATGGATGCTCATAGAAGTTCCTGTCCAGAGACCTGTTCTCTATCCACAAGAGCAAGAAAA TGAGCCATCCATCGGGGAGTTTAATGAGCAGGTTCTGCGACTGATGCACAGCCTTGGAAT AGATCAGCAGAAARCCATTGAGTCTTTGCAGAACAAGAGCTATAACCACTTTGCTGCCAT TTATTTCTTGTTGGTGGAGCGCCTGAAATCACATCGGAGCAGTTTCCCAGTGGAGCAGAG ACTTGATGGCCGCCAGCGTCGGCCTAGCACCATTGCTGAGCAAACAGTTGCCAAGGCACA GACTGTGGGGCTCCCAGTGACCATGCATTCACCGAACATGAGGCTGCTGCGATCTGCCCT CCTCCCCAGGCATCCAACGTGGAGGCCTTTTCATTTCCAGCATCTGGCTGTCAGGCGGA AGCTGCATTCATGGAAGAAGAGTGTGTGGACACTCCAAAGGTCAATGGCTGTCTGCTTGA CCCTGTGCCTCCTGTCCTGGTGCGGAAGGGATGCCAGTCACTGCCCAGCAACATGATGGA GACCTCCATTGACGAAGGGCTGGAGACAGAAGGAGAGGCCCGAGGAAGACCCCGCTCATGC CTTTGAGGCATTTCAGTCCACACGCAGCGGGCAGAGACGGCACACTCTGTCAGAAGTGAC CCTTGACAGTGTGGACTCTGAGTATGATATGGGGTCTGTTCAGAGGGACCTGAACTTTCT GGAAGACAACCCTTCCCTTAAGGACATCATGTTAGCCAATCAGCCTTCACCCCGCATGAC ATCTCCCTTCATAAGCCTGAGACCTACCAACCCAGCCATGCAGGCTCTGAGCTCCCAGAA ACGAGAGGTCCACAACAGGTCTCCAGTGAGCTTCAGAGAGGGCCCGCAGAGCATCAGATAC CTCCCTCACCCAGGGAATTGTAGCATTTAGACAACATCTTCAGAATCTGGCTAGAACCAA AGGAATTCTAGAGTTGAACAAAGTGCAGTTGTTGTATGAACAAATAGGACCGGAGGCAGA CCCTAACCTGGCGCCGGCGCTCCTCAGCTCCAGGACCTTGCTAGCAGCTGCCCTCAGGA AGAAGTTTCTCAGCAGCAGGAAAGCGTCTCCACTCTCCCTGCCAGCGTGCATCCCCAGCT GTCCCCACGGCAGAGCCTGGAGACCCAGTACCTGCAGCACAGACTCCAGAAGCCCAGCCT TCTGTCAAAGGCCCAGAACACCTGTCAGCTTTATTGCAAAGAACCACCGCGGAGCCTTGA

# FIGURE 2CC

ACTGCAGGCCTATTTTAATCAGATGCAGATAGCAGAGGCTCCTACCCACAGCCAAGTCA GCAGCTGCCCCTTCCCCGCCAGGAGACTCCACCGCCTTCTCAGCAGGCCCCACCGTTCAG CCTGACCCAGCCCCTGAGCCCCGTCCTGGAGCCTTCCTCCGAGCAGATGCAATACAGCCC TTTCCTCAGCCAGTACCAAGAGATGCAGCTTCAGCCCCTGCCCTCCACTTCCGGTCCCCG GGCTGCTCCTCTCTCCCACGCAGCTACAGCAGCAGCAGCCGCCACCGCCACCCCCC TCCACCACCACGACAGCCAGGAGCTGCCCCAGCCCCTTACAGTTCTCCTATCAGACTTG TGAGCTGCCAAGCGCTGCTTCCCCTGCGCCAGACTATCCCACTCCCTGTCAGTATCCTGT GGATGGAGCCCAGCAGAGCGACCTAACGGGGCCAGACTGTCCCAGAAGCCCAGGACTGCA AGAGGCCCCTCCAGCTACGACCCACTAGCCCTCTCTGAGCTACCTGGACTCTTTGATTG TGAAATGCTAGACGCTGTGGATCCACAACACACGGGTATGTCCTGGTGAATTAGTCTCA GCACAGGAATTGAGGTGGGTCAGGTGAAGGAAGAGTGTATGTTCCTATTTTTATTCCAGC CTTTTAAATTTAAAGCTTATTTTCTTGCCCTCTCCCTAACGGGGAGAAATCGAGCCACCC AACTGGAATCAGAGGGTCTGGCTGGGGTGGATGTTGCTTCCTCCTGGTTCTGCCCCACCA CAAAGTTTTCTGTGGCAAGTGCTGGAACATAGTTGTAGGCTGAGGCAGGAGAATGGCGTG AACCCGGGAGCCGGAGCTTGCAGTGAGCCAAGATCGTGCCACTGCACTCCAGCCTGGGCG ACTGAGCAAGACTCCACCTCAAAAAAAAAAAAAAAGGACAAGAGCAGTATCATCTGCCTC TGTTTCTAAACTGGACAAAGAGATTTTCTTAAAGTTTCTATCATCTCCCTTCTGACAGGT TCTACAGTGTGGTCTGAAGCACCTGTAATGTCAGAGCCCTTGTCTGGCCCTTGGTGGCAG GTGAACGAAAGCAGTGGAGCCTCTCACCTTCCAGTAGCCTCTCACATTCTTATTTTACCA TTTTTGTCCTAATTAAGGTAGCCTAGCTGATTCTAGAAGACAGCCATCCTACGTGCACCC CCACCTTGTGTCCACATCTTCTCCAGGCAGGTTTCAACCTATCAGCAGACTCAGGCACAC TGTGATGGGTTCTGCCCAGATACTCTGCTCGCCCACCACAAGGGAGCAATAGCTTATAT TTGTACATTAGTTTTACCAAGCACTTTCTCTTCTAACCCTCACAACAATTCTATGAAATT AGCTGGGGAGATACTGTCCTTATTTTTCACAGCTGAAGAAACCAAAGCTTTGGGAAGTTT GTGACTTCTCTGAGATCACAGCTGGTGATAGAAGGAGCTGGGACACGCGCTTGGGTTGAC TGGCTTCTGGTTTTGGTTCTCTGGCTTCTAGTGCTGGAAGAAGCCCTCTCTTTCCCTTCT CTTTCCTCAGTAGCATCTGACTCTTTTCATAAGCAAACAGCTGTATAAACAAAGCCCCCA TTTTGGTCAAGCACAGGGTGAATGTGATATTGTTCCCACAACCTTATTCTCCACTCAACA GCCGCCTGGCTTTGGGGAAGAGGCCGCCTTCAGGTGACAGTGCAGCTGTCCAGGTGGCCG AGTTAACTGCAGAAGTTTAGGCTCACCTCAAAGATGTCTAGTTTTTCCAAGTTACAATAC AGCAGTTTCCTACAGAACACCCCCTTCCTCAATTGCCAAGGGGCCGCATCGCACGGCATC AGGCCACCACTGCAGGCCAGCAGATTCCACCCCAGGAACGGTCATGAACTCAGCCTTTGT CTCAACGAGGGGCGTAACATTTCCTTACAGTCAAGCCCCATCAACTAGAAGTGCTTATTA CTTTTAGGATTAAAAAAGTAATAACAGACTTTGACTTAATACTCTGTCTTTTCAGAGGCA AAGTGGGTGGGTAGAGGGGAGCTTTAAAAATAGAAGTACAAAACAACATCCTGGAAACAT ATGACCCCAGATGGAATAATGTCACATTCCCCAGTGCAGATAATGGGCTGCTGCTGCTC TGTGGTGTCTGCCAGAAGATTTGCTCAGTCAAGGAAATTCAAGTGGTGAGACCTTTC CACCATGGGTGGTAAGAGAAACCTGCCTTCACCAAAATCTCTGAAGGGGAAAGAAGTGGA GAGAAAGGTTTGCTTCACTTCGGGGACTGCAGTTTGAGAAATAAAAGGGATACAGAGATA TGCTGGATGTTTGGTCTGAAAGAGTTACTTTTGATAAAGTTAATCTAATTGTAGTTATAT TTTCTGTGTGCTTTTTTTTAATTACTAAGAAAAAATTGGTGAGTTCAGTAGCTTTGGTA AATTTAAATGGGGTAATTTTCTGCAAGGAAAATGTACTGTTTTTATGTTTCCAACCCTCT **TGA** 

### FIGURE 2DD

SEQ ID NO: 39 AA207220 H GCTGTGGCTCCCGTCCTGGTGCGGGACCTGTGCCCCGCGCTTCAGCCCTCCCCGCAAGC CTATTGATTCCCCTGCCGCCCTTGCTCCACCTCCTGCTCGCCATGGAGTCGCTGGTTTTC CTGATCAAGTCGCCCAAGCCCCTAATGAAGAAGCAGGCGGTGAAGCGGCACCACCACAAG CACAACCTGCGGCACCGCTACGAGTTCCTGGAGACCCTGGGCAAAGGCACCTACGGGAAG GTGAAGAAGGCGCGGGAGAGCTCGGGGCGCCTGGTGGCCATCAAGTCAATCCGGAAGGAC CTCAACCACCCTCACATCATTGCCATCCATGAAGTGTTTGAGAACAGCAGCAAGATCGTG CTCAGTGAGCGCGAAGCTAGGCATTTCTTCCGGCAGATCGTCTCTGCCGTGCACTATTGC CATCAGAACAGAGTTGTCCACCGAGATCTCAAGCTGGAGAACATCCTCTTGGATGCCAAT GGGAATATCAAGATTGCTGACTTCGGCCTCTCCAACCTCTACCATCAAGGCAAGTTCCTG CAGACATTCTGTGGGAGCCCCCTCTATGCCTCGCCAGAGATTGTCAATGGGAAGCCCTAC ACAGGCCCAGAGGTGGACAGCTGGTCCCTGGGTGTTCTCCTCTACATCCTGGTGCATGGC ACCATGCCCTTTGATGGGCATGACCATAAGATCCTAGTGAAACAGATCAGCAACGGGGCC TACCGGGAGCCACCTAAACCCTCTGATTGCCTGNNTGGCCTGATCCGGTGGCTGTTGATG GTGAACCCCACCCGCGGGCCACCCTGGAGGATGTGGCCAGTCACTGGTGGGTCAACTGG GGCTACGCCACCCGAGTGGGAGAGCAGGAGGCTCCGCATGAGGGTGGGCACCCTGGCAGT GACTCTGCCCGCGCCTCCATGGCTGACTGGCTCCGGCGTTCCTCCCGCCCCCTCCTGGAG AATGGGGCCAAGGTGTGCAGCTTCTTCAAGCAGCATGCACCTGGTGGGGGAAGCACCACC CCTGGCCTGGAGCGCCAGCATTCGCTCAAGAAGTCCCGCAAGGAGAATGACATGGCCCAG TCTCTCCACAGTGACACGGCTGATGACACTGCCCATCGCCCTGGCAAGAGCAACCTCAAG CTGCCAAAGGGCATTCTCAAGAAGAAGGTGTCAGCCTCTGCAGAAGGGGTACAGGAGGAC CCTCCGGAGCTCAGCCCAATCCCTGCGAGCCCAGGGCAGGCTGCCCCCTGCTCCCCAAG AAGGGCATTCTCAAGAAGCCCCGACAGCGCGAGTCTGGCTACTACTCCTCTCCCGAGCCC AGTGAATCTGGGGAGCTCTTGGACGCAGGCGACGTGTTTGTGAGTGGGGATCCCAAGGAG CAGAAGCCTCCGCAAGCTTCAGGGCTGCTCCTCCATCGCAAAGGCATCCTCAAACTCAAT GGCAAGTTCTCCCAGACAGCCTTGGAGCTCGCGGCCCCCACCACCTTCGGCTCCCTGGAT GAACTCGCCCCACCTCGCCCCTGGCCCGGGCCAGCCGACCCTCAGGGGCTGTGAGCGAG GACAGCATCCTGTCCTCTGAGTCCTTTGACCAGCTGGACTTGCCTGAACGGCTCCCAGAG CCCCACTGCGGGGCTGTGTGTCTGTGGACAACCTCACGGGGCTTGAGGAGCCCCCCTCA GAGGGCCCTGGAAGCTGCCTGAGGCGCTGGCGGCAGGATCCTTTGGGGGACAGCTGCTTT TCCCTGACAGACTGCCAGGAGGTGACAGCGACCTACCGACAGGCACTGAGGGTCTGCTCA AAGCTCACCTGAGTGGAGTAGGCATTGCCCCAGCCCGGTCAGGCTCTCAGATGCAGCTGG TTGCACCCGAGGGGAGATGCCTTCTCCCCCACCTCCCAGGACCTGCATCCCAGCTCAGA AGGCTGAGAGGGTTTGCAGTGGAGCCCTGAGCAGGGCTGGATATGGGAAGTAGGCAAATG AAATGCGCCAAGGGTTCAGTGTCTGTCTTCAGCCCTGCTGAACGAAGAGGATACTAAAGA GAGGGGAACGGGAATGCCCGCGACAGAGTCCACATTGCCTGTTTCTTGTGTACATGGAGG **GGCCACAGAGA** 

### FIGURE 2EE

TCCGAAGCCCGCAGATACATCCGACAGCTCATCTCTGCCGTAGAGCACCTGCACCGGGCC GGGGTGGTCCACAGAGACTTGAAGATAGAGAATTTGCTACTAGATGAAGACAATAATATC AAGCTGATTGACTTTGGTTTGAGCAACTGCGCAGGGATCCTGGGTTACTCGGATCCGTTC AGCACACAGTGTGGCAGCCTGCCTACGCTGCACCTGAACTGCTCGCCAGGAAGAAATAC GGCCCCAAAATCGATGTCTGGTCCATAGGTGTGAACATGTATGCCATGTTGACCGGGACG CTGCCTTTCACGGTGGAGCCTTTCAGCCTGAGGGCTTTGTACCAGAAGATGGTAGACAAA GAAATGAACCCCCTCCCCACTCAGCTCTCCACAGGTGCCATCAGTTTCCTGCGCTCTCTC CTGGAACCGGATCCTGTGAAGAGGCCAAATATTCAGCAGGCACTGGCGAATCGCTGGCTT AATGAGAATTACACGGGCAAAGTGCCCTGTAATGTCACCTATCCCAACAGGATTTCTCTG GAAGATCTGAGCCCGAGCGTCGTGCTGCACATGACCGAGAAGCTGGGTTACAAGAACAGC GACGTGATCAACACTGTGCTCTCCAACCGCGCCTGCCACATCCTGGCCATCTACTTCCTC TTAAACAAGAAACTGGAGCGCTATTTGTCAGGGAAATCTGACATCCAGGACAGCCTCTGC TACAAGACCCGGCTCTACCAGATAGAAAAGTACAGGGCCCCCAAGGAGTCCTATGAGGCC TCTCTGGACACCTGGACACGAGATCTTGAATTCCATGCCGTGCAGGATAAAAAGCCCCAAA GAACAAGAAAAAGAGGGGATTTTCTTCATCGACCATTCTCCAAGAAGTTGGACAAGAAC CTGCCCTCGCACAAACAGCCCTCAGGCTCGCTTATGACACAGATTCAGAACACCAAAGCC CTCCTGAAGGACCGGAAGGCCTCCAAGTCCAGCTTCCCCGACAAAGATTCCTTTGGCTGC CGCAATATTTTCCGCAAAACCTCAGATTCCAATTGTGTGGCTTCTTCTTCCATGGAGTTC ATCCCCGTGCCACCGCCCAGGACCCCGAGGATTGTGAAGAAACCGGAGCCCCATCAGCCA GGGCCCGGAAGCACTGGCATCCCCCACAAGGAAGACCCCCTGATGCTGGACATGGTGCGC TCCTTCGAGTCTGTGGATCGCGACGACCACGTAGAAGTGCTGTCTCCCTCTCATCACTAC AGGATTCTGAACTCCCCGGTCAGCTTGGCTCGCAGAAATTCCAGCGAGAGGACGCTGTCC CCGGGTCTGCCATCCGGAAGCATGTCGCCTCTCCATACTCCTTTGCATCCAACTCTGGTC TCTTTTGCTCACGAAGATAAGAACAGCCCCCCAAAAGAGGGGGGCCTGTGTTGCCCACCT CCGGTTCCCAGCAATGGCCCCATGCAGCCTCTGGGGAGCCCCAATTGTGTGAAAAGCCGA GGCCGGTTCCCTATGATGGGCATCGGACAGATGTTAAGGAAGCGCCATCAGAGTCTGCAG CCATCTGCAGATAGGCCCCTGGAGGCCAGCCTGCCCCCACTGCAGCCCCTAGCCCCTGTG AACCTTGCCTTTGACATGGCCGATGGGGTCAAGACCCAGTGCTAA

SEQ ID NO: 41\_Z36720 H

ATGGACACAAGCTGAACATGCTGAACGAGAAGGTGGACCAGCTCCTGCACTTCCAAGAA GATGTCACAGAGAAGTTGCAGAGCATGTGCCGAGACATGGGCCACCTGGAGCGGGCCTG GACACCCAGGCTGGGTGGCCCGAGGTCCTGGAGCTGGTGAGGGCCATGCAGCAGGATGCG GCCCAGCACGGTGCCAGGCTGGAGGCCCTCTTCAGGATGGTGGCTGCGGTGGACAGGGCC ATCGCTTTGGTGGGGGCCACGTTCCAGAAATCAAAGGTGGCGGATTTCCTCATGCAGGGG CGTGTGCCCTGGAGGAGAGGCAGCCCAGGTGACAGCCCTGAGGAGTGGGTAAAAGAGGAG GAGGTCTGTTTCATGCCTCCAGTTCCCCCAGCTCCGGGGGCAGCAGGACAGAGCCTGCAG AAGGATAAGGGGGAGCTGTCTGCCGAGCAGGGGATCTGGGCCACATTGATGACGCTGGTG ATCATGGTGACAGCGGCAAATAAAGAGCGAGTGGAAGAAGAGGGGAGGAAAACCAAAGCAT GTGCTGAGCACCAGTGGGGTGCAGTCTGATGCCAGGGAGCCTGGGGAAGAGAGCCAGAAG GCGGACGTGCTGGAGGGGACAGCGGAGAGGCTGCCCCCCATCAGAGCGTCAGGGCTGGGA GCTGACCCCGCCCAGGCAGTGGTCTCACCGGGCCAGGGAGATGGTGTTCCTGGCCCAGCC CAGGCATTCCCTGGCCACCTGCCCCACAAAGGTGGAAGCCAAGGCTCCTGAGACA CCCAGCGAGAACCTCAGGACTGGCCTGGAATTGGCTCCAGCACCCGGCAGGGTCAATGTG GTCTCCCCGAGCCTGGAGGTTGCACCAGGTGCAGGACAAGGAGCATCGTCCAGCAGGCCT GACCCTGAGCCCTTAGAGGAAGGCACGAGGCTGACTCCAGGGCCTGGCCCTCAGTGCCCA GGGCCTCCAGGGCTGCCAGCCCAGGCCAGGGCAACCCACAGTGGTGGAGAAACACCTCCA AGGGCAGCCCTGCTGAAGGGCGCTGTGGCCCCGGGCTTCTCTCGGAGGGACCTGGTGTTT CCTAGCATCTTCTGCGCCTGCCTAGGGATCTCCATCCACATACAAGAGATGGATACTCCT

### **FIGURE 2FF**

GCAGCTGCCCAGCCAGGCAAGCAGGGCCCACCTGGGACCGGGCGCTGCCTCCAAGCCCCT GGGACTGAGCCCGGAGAACAGACCCCTGAAGGAGCCCAGAGAGCTCTCCCCGCTGCAGGAG AGCAGCAGCCCCGGGGGAGTGAAGGCAGAGGAGGAGCAAAGGGCTGGGGCCGAGCCTGGC ACGAGACCAAGCTTGGCCAGGAGTGACGACAATGACCACGAGGTTGGGGCCCTGGGCCTG CAGCAGGGCAAAAGCCCAGGGGCGGGAAACCCTGAGCCTGAGCAGGACTGTGCAGCCAGG GCTCCGGTGAGAGCTGAAGCAGTAAGGAGGATGCCCCCAGGCGCCGAGGCTGGCAGCGTG GTTCTGGATGACAGTCCGGCCCCACCAGCTCCTTTTGAACACCGGGTAGTGAGCGTCAAG GAGACCTCCATCTCTGCGGGTTACGAGGTGTGCCAGCACGAAGTCTTGGGAGGGGGTCGG TTTGGCCAGGTCCACAGGTGCACAGAGAAGTCCACAGGCCTCCCACTGGCTGCCAAGATC ATCAAAGTGAAGAGCGCCAAGGACCGGGAGGACGTGAAGAACGAGATCAACATCATGAAC ACCCTTGTCATGGAGTACGTGGACGGGGTGAGCTCTTCGACCGGATCACAGATGAGAAG TACCACCTGACTGAGCTGGATGTGGTCCTGTTCACCAGGCAGATCTGTGAGGGTGTGCAT TACCTGCACCAGCACTACATCCTGCACCTGGACCTCAAGCCGGAGAACATATTGTGCGTC AATCAGACAGGACATCAAATTAAGATCATTGACTTTGGGCTGGCCAGAAGGTACAAGCCT CGAGAGAAGCTGAAGGTGAACTTCGGCACTCCTGAGTTCCTGGCCCCAGAAGTCGTCAAT TATGAGTTTGTCTCATTCCCCACAGACATGTGGAGTGTGGGAGTCATCACCTACATGCTA CTCAGTGGCTTGTCCCCATTTCTAGGGGAAACAGATGCAGAGACCATGAATTTCATTGTA AACTGTAGCTGGGATTTTGATGCTGACACCTTTGAAGGGCTCTCGGAGGAGGCCAAGGAC TTTGTTTCCCGGTTGCTGGTCAAAGAGAAGAGCTGCAGAATGAGTGCCACACAGTGCCTG AAACACGAGTGGCTGAATAATTTGCCTGCCAAAGCTTCAAGATCCAAAACTCGTCTCAAA TCCCAACTACTGCTGCAGAAATACATAGCTCAAAGAAAATGGAAGAAACATTTCTATGTG GTGACTGCTGCCAACAGGTTAAGGAAATTTCCAACTTCTCCCTAA

# SEO ID NO: 42 SGK088 H

GGGGAGATGGCGTGTTTGAGTGCCTGGTGGCGGGCCCACTGACGTGGAGGTGGATTGG CTGTGCCGTGGCCGCCTGCAGCCTGCACTGCTCAAATGCAAGATGCATTTCGATGGC CGCAAATGCAAGCTGCTACTTACATCTGTACATGAGGACGACAGTGGCGTCTACACCTGC AAGCTCAGCACGGCCAAAGATGAGCTGACCTGCAGTGCCCGGCTGACCGTGCGGCCCTCG TTGGCACCCCTGTTCACACGGCTGCTGGAAGATGTGGAGGTGTTGGAGGGCCGAGCTGCC CGTTTCGACTGCAAGATCAGTGGCACCCCGCCCCCTGTTGTTACCTGGACTCATTTTGGC CACATTGCCCATGTGGGCAGCGAGGACGAGGGGCTCTATGCGGTCAGTGCTGTTAACACC CATGGCCAGGCCCACTGCTCAGCCCAGCTGTATGTAGAAGAGCCCCCGGACAGCCGCCTCA GGCCCCAGCTCGAAGCTGGAGAAGATGCCATCCATTCCCGAGGAGCCAGAGCAGGGTGAG CTGGAGCGGCTGTCCATTCCCGACTTCCTGCGGCCACTGCAGGACCTGGAGGTGGGACTG GCCAAGGAGGCCATGCTAGAGTGCCAGGTGACCGGCCTGCCCTACCCCACCATCAGCTGG TTCCACAATGGCCACCGCATCCAGAGCAGCGACCGCCGCGCATGACACAGTACAGGGAT GTCCATCGCTTGGTGTTCCCTGCCGTGGGGCCTCAGCACGCCGGTGTCTACAAGAGCGTC ATTGCCAACAAGCTGGGCAAAGCTGCCTGCTATGCCCACCTGTATGTCACAGATGTGGTC CCAGGCCCTCCAGATGGCGCCCCGCAGGTGGTGGCTGTGACGGGGAGGATGGTCACACTC ACATGGAACCCCCCCAGGAGTCTGGACATGGCCATCGACCCGGACTCCCTGACGTACACA GTGCAGCACCAGGTGCTGGGCTCGGACCAGTGGACGGCACTGGTCACAGGCCTGCGGGAG CCAGGGTGGGCAGCCACAGGGCTGCGTAAGGGGGTCCAGCACATCTTCCGGGTCCTCAGC ACCACTGTCAAGAGCAGCAGCAAGCCCTCACCCCCTTCTGAGCCTGTGCAGCTGCTGGAG CACGGCCCAACCCTGGAGGAGGCCCCTGCCATGCTGGACAAACCAGACATCGTGTATGTG GTGGAGGGACAGCCTGCCAGCGTCACCGTCACATTCAACCATGTGGAGGCCCAGGTCGTC TGGAGGAGCTGCCGAGGGGCCCTCCTAGAGGCACGGGCCGGTGTGTACGAGCTGAGCCAG CCAGATGATGACCAGTACTGTCTTCGGATCTGCCGGGTGAGCCGCCGGGACATGGGGGCC

# FIGURE 2GG

CTCACCTGCACCGCCCGAAACCGTCACGGCACACAGACCTGCTCGGTCACATTGGAGCTG GCAGAGGCCCCTCGGTTTGAGTCCATCATGGAGGACGTGGAGGTGGGGGCTGGGGAAACT GCTCGCTTTGCGGTGGTCGAGGGAAAACCACTGCCGGACATCATGTGGTACAAGGAC GAGGTGCTGACCGAGAGCAGCCATGTGAGCTTCGTGTACGAGGAGAATGAGTGCTCC CTGGTGGTGCTCAGCACGGGGGCCCAGGATGGAGGCGTCTACACCTGCACCGCCCAGAAC CTGGCGGGTGAGGTCTCCTGCAAAGCAGAGTTGGCTGTGCATTCAGCTCAGACAGCTATG GACATCCACCAGGAGATCGGCAGGGGTGCTTTCTCCTACTTGCGGCGCATAGTGGAGCGT GCGCGTCGGGAGGCCCGGCTGCTGGCCAGGCTCCAGCACGACTGTGTCCTCTACTTCCAT GAGGCCTTCGAGAGGCGCCGGGGACTGGTCATTGTCACCGAGCTCTGCACAGAGGAGCTG CTGGAGCGAATCGCCAGGAAACCCACCGTGTGTGAGTCTGAGATCCGGGCCTATATGCGG CAGGTGCTAGAGGGAATACACTACCTGCACCAGAGCCACGTGCTGCACCTCGATGTCAAG CCTGAGAACCTGCTGGTGTGGGATGGTGCTGCGGGCGAGCAGCAGGTGCGGATCTGTGAC TTTGGGAATGCCCAGGAGCTGACTCCAGGAGAGCCCCAGTACTGCCAGTATGGCACACCT GAGTTTGTAGCACCCGAGATTGTCAATCAGAGCCCCGTGTCTGGAGTCACTGACATCTGG CCTGTGGGTGTTGTTGCCTTCTCTGTCTGACAGGAATCTCCCCGTTTGTTGGGGAAAAT GACCGGACAACATTGATGAACATCCGAAACTACAACGTGGCCTTCGAGGAGACCACATTC CTGAGCCTGAGCAGGGAGGCCCGGGGCTTCCTCATCAAAGTGTTGGTGCAGGACCGGCTG AGACCTACCGCAGAAGAGACCCTAGAACATCCTTGGTTCAAAACTCAGGCAAAGGGCGCA GAGGTGAGCACGGATCACCTGAAGCTATTCCTCTCCCGGCGGAGGTGGCAGCGCTCCCAG ATCAGCTACAAATGCCACCTGGTGCTGCGCCCCATCCCCGAGCTGCTGCGGGCCCCCCCA GAGCGGGTGTGGGTGACCATGCCCAGAAGGCCACCCCCAGTGGGGGGCTCTCATCCTCC TCGGATTCTGAAGAGGAAGAGCTGGAAGAGCTGCCCTCAGTGCCCCGCCCACTGCAGCCC GAGTTCTCTGGCTCCCGGGTGTCCCTCACAGACATTCCCACTGAGGATGAGGCCCTGGGG ACCCCAGAGACTGGGGCTGCCACCCCCATGGACTGGCAGGAGCAGGGAAGGGCTCCCTCT CAGGACCAGGAGGCTCCCAGCCCAGAGGCCCTCCCCCAGGCCAGGAGCCCGCAGCT GGGGCTAGCCCCAGGCGGGAGAGCTCCGCAGGGGCAGCTCGGCTGAGAGCGCCCTGCCC CGGGCCGGGCCGGGGCCTGCACAAGGCGGCGTCTGTGGAGCTGCCG CAGCGCCGGAGCCCCGGGAGCCACCCGCCTGGCCCGGGGAGGCCTGGGTGAGGGC GAGTATGCCCAGAGGCTGCAGGCCCTGCGCCAGCGGCTGCTGCGGGGAGGCCCCGAGGAT GGCAAGGTCAGCGCCTCAGGGGTCCCCTGCTGGAGAGCCTGGGGGGCCGTGCTCGGGAC CCCCGGATGGCACGAGCTCCCAGCGAGGCAGCGCCCCACCAGCCCCCACTCGAG AACCGGGGCCTGCAAAAGAGCAGCAGCTTCTCCCAGGGTGAGGCGGAGCCCCGGGGCCGG CACCGCCGAGCGGGGGCCCCCTCGAGATCCCCGTGGCCAGGCTTGGGGCCCGTAGGCTA CAGGAGTCTCCTTCCCTGTCTGCCCTCAGCGAGGCCCAGCCATCCAGCCCTGCACGGCCC GCTCCGCAGCCCCCGCACCCCAGCCTGCCCAAGACAAGGCTCCAGAGCCCAGGCCAGAA CCAGTCCGAGCCTCCAAGCCTGCACCACCCCCCAGGCCCTGCAAACCCTAGCGCTGCCC CTCACACCCTATGCTCAGATCATTCAGTCCCTCCAGCTGTCAGGCCACGCCCAGGGCCCC TCGCAGGGCCCTGCCGCCCCCTTCAGAGCCCCAAGCCCCACGCTGCTGTTTTGCCAGG GTGGCCTCCCCACCTCCGGGAGCCCCCGAGAAGCGCGTGCCCTCAGCCGGGGGTCCCCCG GTGCTAGCCGAGAAAGCCCGAGTTCCCACGGTGCCCCCAGGCCAGGCAGCAGTCTCAGT AGCAGCATCGAAAACTTGGAGTCGGAGGCCGTGTTCGAGGCCAAGTTCAAGCGCAGCCGC GAGTCGCCCTGTCGCTGGGGCTGCGGCTGCTGAGCCGTTCGCGCTCGGAGGAGCGCGGC CCCTTCCGTGGGGCCGAGGAGGAGGATGGCATATACCGGCCCAGCCCGGCGGGGACCCCG CTGGAGCTGGTGCGACGCCTGAGCGCTCACGCTCGGTGCAGGACCTCAGGGCTGTCGGA GAGCCTGGCCTCGCCGCCTCTCGCTGTCACTGTCCCAGCGGCTGCGGCGGACCCCT CCCGCGCAGCCCCCGGCCTGGGAGGCCCGCGGGGGGACGGAGAGCTCGGAGGGC GGGAGCTCGGCGGGGCTCCCCGGTGCTGGCGATGCGCAGGCGGCTGAGCTTCACCCTG

61/119

### FIGURE 2HH

GAGCGGCTGTCCAGCCGATTGCAGCGCAGTGGCAGCAGCGAGGACTCGGGGGGCGCGTCG GGCCGCAGCACGCCGCTGTTCGGACGGCTTCGCAGGGCCACGTCCGAGGGCGAGAGTCTG CGGCGCCTTGGCCTTCCGCACAACCAGTTGGCCGCCCAGGCCGCCCACCACGCCTTCC GCCGAGTCCCTGGGCTCCGAGGCCAGCGCCACGTCGGGCTCCTCAGCCCCAGGGGAAAGC  $\tt CGAAGCCGGCTCCGCTGGGGCTTCTCTCGGCCGCGGAAGGACAAGGGGTTATCGCCACCA$ AACCTCTCTGCCAGCGTCCAGGAGGAGTTGGGTCACCAGTACGTGCGCAGTGAGTCAGAC ACCCTGCTCTGCCAGCGGCCTGCCCTGCACCGCACATCTCCTGGATGAAAGACAAG AAGTCCTTGAGGTCAGAGCCCTCAGTGATCATCGTGTCCTGCAAAGATGGGCGGCAGCTG CTCAGCATCCCCGGGCGGGCAAGCGGCACGCCGGTCTCTATGAGTGCTCGGCCACCAAC GTACTGGGCAGCATCACCAGCTCCTGTACCGTGGCTGTGGCCCGAGTCCCAGGAAAGCTA GCTCCTCCAGAGGTAACCCAGACCTACCAGGACACGGCGCTGGTGCTGTGGAAGCCGGGA GACAGCCGGGCACCTTGCACGTATACGCTGGAGCGGCGAGTGGATGGGGAGTCTGTGTGG CACCCTGTGAGCTCAGGCATCCCCGACTGTTACTACAACGTGACCCACCTGCCAGTTGGC GTGACTGTGAGGTTCCGTGTGGCCTGTGCCAACCGTGCTGGGCAGGGGCCCCTTCAGCAAC TCTTCTGAGAAGGTCTTTGTCAGGGGTACTCAAGATTCTTCAGCTGTGCCATCTGCTGCC CACCAAGAGGCCCCTGTCACCTCAAGGCCAGCCAGGGCCCGGCCTCCTGACTCTCCTACC TCATCTCCCCCCACACCTCCTAGCCAGGCCTTGTCCTCGCTCAAGGCTGTGGGTCCACCA CCCCAAACCCCTCCACGAAGACACAGGGGCCTGCAGGCTGCCCGGCCAGCGGAGCCCACC CTACCCAGTACCCACGTCACCCCAAGTGAGCCCAAGCCTTTCGTCCTTGACACTGGGACC CCGATCCCAGCCTCCACTCCTCAAGGGGTTAAACCAGTGTCTTCCTCTACTCCTGTGTAT GTGGTGACTTCCTTTGTGTCTGCACCACCAGCCCCTGAGCCCCAGCCCCTGAGCCCCCT CCTGAGCCTACCAAGGTGACTGTGCAGAGCCTCAGCCCGGCCAAGGAGGTGGTCAGCTCC CCTGGGAGCAGTCCCCGAAGCTCTCCCAGGCCTGAGGGTACCACTCTTCGACAGGGTCCC CCTCAGAAACCCTACACCTTCCTGGAGGAGAAAGCCAGGGGCCGCTTTGGTGTTGTGCGA GCGTGCCGGGAGAATGCCACGGGGCGAACGTTCGTGGCCAAGATCGTGCCCTATGCTGCC GAGGGCAAGCCGCGGGTCCTGCAGGAGTACGAGGTGCTGCGGACCCTGCACCACGAGCGG ATCATGTCCCTGCACGAGGCCTACATCACCCCTCGGTACCTCGTGCTCATTGCTGAGAGC TGTGGCAACCGGGAACTCCTCTGTGGGCTCAGTGACAGGTTCCGGTATTCTGAGGATGAC GTGGCCACTTACATGGTGCAGCTGCTACAAGGCCTGGACTACCTCCACGGCCACCACGTG CTCCACCTAGACATCAAGCCAGACAACCTGCTGCTGGCCCCTGACAATGCCCTCAAGATT GTGGACTTTGGCAGTGCCCAGCCCTACAACCCCCAGGCCCTTAGGCCCCTTGGCCACCGC ACGGGCACGCTGGAGTTCATGGCTCCGGAGATGGTGAAGGGAGAACCCATCGGCTCTGCC ACGGACATCTGGGGAGCGGGTGTGCTCACTTACATTATGCTCAGTGGACGCTCCCCGTTC TATGAGCCAGACCCCCAGGAAACGGAGGCTCGGATTGTGGGGGGCCGCTTTGATGCCTTC CAGCTGTACCCCAATACATCCCAGAGCGCCACCCTCTTCTTGCGAAAGGTTCTCTCTGTA TACCTGATGAAGCTGCGCCGCCAGACGCTCACCTTCACCACCAACCGGCTCAAGGAGTTC CTGGGCGAGCAGCGGCGCGGGCTGAGGCTGCCACCCGCCACAAGGTGCTGCGC TCCTACCCTGGCGGCCCCTAGAGGCACGGACCACAGCCAGGCCTCGGGCTTCAACTGGGG TTCCCACCAATGCCACGGGACATTCCAGGGCCCACGCTGAGCCAGGCGGGCCTGGGGCTT CGGTTACCACCAGCAGCAACATCTGGCTGGGCTCTTACCTCATAGACCTTCAAGGACAGA GACCCCAGGGCCTGGACCTGATGCCACCCCAGGCCAAAGCCAGAGTGGGAGACCCATTGG TCAGGCTCAGCAGGGTGGGAACAGGCAGAGGGGACAAGAGGGGGAATGGAGAAGTGGAGAGG AAAAGGAATCGAGGGACAGGAAGGGGGGGGGCTCTAGGAAGGTTCTGGGTTGGGGGTCAGT CCAGGTGTCAGGGCAGTAGGCTGGGAGTCAGTGTGGCAAAGCGGGGGCAGGACACAGATA CAGTGGCAGGGCCCAGGGCTGGGACATGAGAGAAGGCAGCGAGGCGCAGAGGGAGAAG AGAGGACTCAGGTGGAGGTGGGGTGGGTCAGCTGTCAGCATCCCTCAGAGGAGAAATGTG

# FIGURE 2II

SEO ID NO: 43 AA542015 M SGK088 M GCCACGGACATCTGGGGAGCGGGTGTGCTCACCTACATCATGCTTAGTGGGTACTCCCCA TTCTATGAGCCAGACCCCCAGGAAACAGAGGCTCGGATTGTTGGGGGGTCGCTTTGATGCC TTCCAGTTGTATCCTAACACATCCCAGAGTGCCACCCTCTTCTTGAGAAAGGTCCTCTCA GCCTACCTGATGAAGCTGCGCCGCCAGACACTCACCTTCACCACCCAACCGGCTCAAGGAA TTCCTGGGCGAGCAGCGCGACGTCGGGCTGAGGCTGCTACCCGTCACAAGGTGCTGCTC CGCTCCTACCCTGGCAGCCCCTAGGTGGCACAGACCGCAGCCCGGCCACGGGCTTCAACT TGGGTTCTCACTCGCGCTGCCAAGGGACATTCCAGAGCCCATGCTGAGCTGGACAGGCAG ACCTCATGGACCTAAGAGGACAAGGCCCTGGGGCTTCAGCCGAATGTCACCCCGGCCATA ACCAGAGCAGGAGACCCACTGGCCAGGCTGGGCAAGGGTGAGAGCAGAAAGAGCAAAAGA TAGGCTGGAGTGGAATGCTATATCTCAGGGAGAAGCCAGAAGGGGACATGGCTGAAGAGG AAGAAGGACCCTGTGATGTGGGAATGTGGTGGAGAGGAGGACTGGACATAGAGAGTGTGC CAGGAGCCAGAGCAGAGACATAAGGGAGGGCAGAAGGGTAGAAGGCAACAGGAGTGGGCT AGACGAAAGGCCGCTCCAGCTGGTCTCCTGTCCCAGCCGATGCAGTTCTGGGCGTTCTCC ACTGGCCCAGGGATGTCCTCACTGCTCCTCCATGGCCTTTGCCCTCCTTCCCATTTGTAT TTATTTATTTATTGCCTTTTGTGGAGTTTCCTTTCTATCCAGTCCCTAGTGCCTATGTTG 

SEQ ID NO: 44 R19772\_H ATGAAGGGCGGCGACAGGGCTTACACCCGAGGTCCCTCTTTGGGGTGGCTCTTTGCTAAG TGCTGCTGTTGCTTCCCGTGTAGAGATGCATACTCTCATTCCTCAAGCGAGAATGGAGGC -CCGGGTCCCAAGCGCTCCACCAACACTCTTAAGAAGTGGCTGACGAGTCCTGTGCGTCGG CTCAACAGCGGGAAGGCAGATGGAAACATCAAAAAGCAGAAGAAAGTTCGCGATGGTCGG AAGAGCTTTGACCTGGGATCTCCCAAGCCTGGGGATGAAACAACCCCTCAGGGAGACAGC GCTGATGAGAGCAAGAAAGGTTGGGGTGAAGATGAGCCGGATGAAGAGTCACACACCC CTCCCACCACCTATGAAGATTTTTGACAACGACCCTACACAGGATGAAATGTCCTCCTCT TTGCTAGCAGCCCGGCAGGCTTCCACTGAAGTACCTACTGCTGCAGACCTTGTCAATGCA GAAGAAGAACAGAAAGCCAAGGCCCTGAGAGGCAGGATGTTTGTCCTGAATGAGCTGGTA CAGACAGAGAAAGACTATGTCAAGGATCTGGGCATTGTGGTGGAGGGCTTCATGAAGAGA ATAGAAGAAAAGGGTGTCCCTGAGGATATGCGAGGAAAGGACAAAATCGTGTTTGGAAAT ATTCATCAGATTTATGACTGGCATAAGGATTTTTTCCTGGCGGAACTGGAAAAGTGTATC CAGGAGCAAGACAGATTGGCACAGCTCTTTATTAAGCACGAGCGGAAGCTGCACATCTAC GTGTGGTATTGTCAGAATAAGCCGCGCTCAGAGTACATCGTTGCTGAGTATGACGCCTAC TTTGAGGAGGTAAAACAGGAGATAAATCAGAGGCTGACACTGAGTGACTTCCTCATCAAG CCCATTCAGAGAATAACAAAATACCAGTTGCTCCTCAAGGACTTCCTGAGATACAGTGAG AAGGCTGGTTTGGAGTGTTCAGATATCGAGAAAGCAGTGGAGTTAATGTGCCTTGTTCCC

### FIGURE 2JJ

AAACGCTGCAATGACATGATGAATCTAGGACGTCTGCAGGGCTTTGAGGGCACTCTGACT GCTCAGGGGAAGCTACTGCAGCAGGACACATTCTATGTGATCGAGCTGGATGCAGGCATG CAGTCCCGGACCAAAGAGAGGCGCGTGTTCCTCTTCGAGCAGATTGTCATCTTCAGTGAA CTGCTCAGGAAGGGATCCCTCACCCCTGGCTACATGTTCAAAAGGAGCATCAAGATGAAT TACTTGGTCCTGGAGGAGAATGTGGACAATGATCCCTGCAAGTTTGCACTCATGAACAGA GAGACTTCTGAGAGGGTTGTTCTGCAAGCCGCCAACGCTGACATCCAGCAGGCCTGGGTG CAGGACATCAATCAAGTCTTAGAAACACAGCGAGACTTTTTGAATGCACTGCAATCGCCC ATTGAGTATCAACGGAAAGAAGGAGCACAGCTGTGATGAGGTCTCAACCTGCCAGGCTT CCCCAAGCCAGCCCCAGGCCCTACTCCTCTGTTCCTGCGGGCTCAGAGAAGCCCCCAAAG GGCTCCAGCTATAACCCACCTCTGCCTCCCCTGAAGATATCTACCTCCAATGGCAGTCCA GGGTTTGAATACCACCAGCCTGGGGACAAGTTCGAAGCCAGCAAGAACGACCTGGGAGGC TGCAATGGGACCTCGTCCATGGCCGTGATCAAAGATTACTATGCACTGAAGGAGAATGAA ATCTGTGTGAGCCAAGGTGAGGTGGTCCAGGTCCTCGCCGTCAACCAGCAGAACATGTGT CTGGTGTACCAGCCTGCCAGCGACCATTCCCCCGCCGAGGGCTGGGTCCCAGGCAGC ATCCTGGCGCCCCTCACCAAAGCCACAGCAGCAGAAAGTAGTGACGGGAGCATCAAGAAG AATGAAGCCACAGGGCCTCGTAAACCCAAGGATATTCTGGGCAACAAAGTCTCTGTTAAA GAGACGAACAGTTCCGAGGAATCAGAGTGTGATGATCTTGACCCTAATACTAGCATGGAG ATCTTAAATCCAAATTTCATCCAAGAAGTGGCCCCAGAATTCCTTGTGCCCTTGGTGGAT GTGACCTGCTTGCTTGGGGACACAGTGATACTGCAGTGCAAAGTCTGTGGGCGGCCAAAG CCCACCATCACTTGGAAGGGTCCAGACCAGAACATCCTTGACACTGATAACAGCTCAGCC ACATACACGGTCTCCTCTTGTGATTCTGGAGAAATCACCCTGAAGATCTGTAATCTGATG CCCCAAGACAGTGGGATTTATACCTGCATAGCAACAAATGACCACGGGACCACATCAACG TCTGCAACAGTCAAAGTGCAAGGTGTTCCAGCAGCCCCTAACCGCCCCATTGCCCAGGAG AGAAGCTGCACCTCCGTGATTCTCCGCTGGCTGCCCCCCTCCAGCACAGGAAACTGCACT GCTTCGACCTTGGACACTTACCTCGTCATCGAAGACCTTAGTCCCGGGTGTCCTTATCAG TTCAGAGTCAGTGCCAGTAACCCCTGGGGAATCAGCCTTCCCAGCGAGCCCTCGGAGTTT TTTGACTCAGCTTACACTGAGCTGAATGAAATTGGAAGAGGCCGTTTCTCTATAGTAAAG AAATGCATTCACAAAGCTACCCGCAAAGATGTGGCTGTGAAATTTGTTAACAAAAAAATG AAGAAGAAAGAACAGGCTGCCCACGAGGCTGCCCTGCTTCAGCACCTACAGCACCCCCAG TACATCACTCTCCATGACACCTATGAGTCCCCCACATCCTACATCCTGATCTTGGAACTG ATGGATGATGGCCGGCTCTTAGACTACCTTATGAATCATGATGAACTGATGGAGGAAAAA GTAGCTTTCTATATCCGAGACATCATGGAGGCTCTGCAGTACCTTCACAACTGCAGGGTT GCACATTTGGACATAAAGCCTGAAAACCTGCTCATTGACCTACGGATTCCAGTGCCTCGA GTGAAGCTCATTGACTTGGAGGATGCTGTCCAGATCTCGGGTCACTTCCACATTCACCAC CTGCTGGGGAACCCTGAGTTTGCTGCCCCAGAAGTCATTCAAGGCATCCCCGTCTCCCTG GGGACAGACATCTGGAGCATCGGGGTTCTGACATATGTCATGCTGAGTGGGGTCTCCCCC TTCTTGGATGAGAGCAAAGAGGAGACATGTATCAACGTATGCAGGGTGGATTTCAGCTTC CCCCATGAATACTTCTGTGGTGTGAGCAATGCTGCCAGAGATTTCATCAATGTGATCTTA CAGGAAGATTTTCGGAGGCGGCCCACAGCAGCCACATGCTTGCAGCATCCATGGCTGCAG CCCCATAATGGCAGCTACTCTAAGATCCCCCTGGACACCTCCCGCCTAGCATGCTTCATA GAACGTCGCAAGCACCAGAATGATGTGCGGCCTATCCCCAATGTCAAGAGCTACATTGTC AACCGGGTGAACCAAGGGACGTAG

SEQ ID NO: 45\_5R72\_8\_2\_H CGCCGCTGTTTGTCCTCGCGCGCCCCGTCCACTGCCCTGCGGTTGCTCTGCGGGCTGAA AAGTTTCTCCCGGTGCAGAATTCCGGGCTCAGCGACAGCCTGCGCCGAGTGTGCGCACCT GTCGGAGACCCGCCAGTCCGCCGGCCCCGGCTTTGTTCGTGCGGAACTGTAGTGGTGAGA

# FIGURE 2KK

TGGGCTGTCACGTGTGAATATGTGTCTAGTGCATCCTTAACCTGAGGACTTCACCAGTTC GAAATTACAGTTTTCACCATCAACTACCTTATCCTTTTTGGCCTGGTTTTCTTCCTCAAA CAGTGGAAACATTTTTAAAGTTGCTTTTGTTGCAGAGTTAAACAAATGGCTGATAGTGGC TTAGATAAAAATCCACAAAATGCCCCGACTGTTCATCTGCTTCTCAGAAAGATGTACTT TGTGTATGTTCCAGCAAAACAAGGGTTCCTCCAGTTTTGGTGGTGGAAATGTCACAGACA AACAGAGATATAACCTCCAGGAAAGATTTGCCCTCAAGAACCTCAAATGTAGAGAAAAA GCATCTCAGCAACAATGGGGTCGGGGCAACTTTACAGAAGGAAAAGTTCCTCACATAAGG ATTGAGAATGGAGCTGCTATTGAGGAAATCTATACCTTTGGAAGAATATTGGGAAAAAGGG AGCTTTGGAATAGTCATTGAAGCGACAGACAAGGAAACAGAAACGAAGTGGGCAATTAAA AAAGTGAACAAAGAAAAGGCTGGAAGCTCTGCTGTGAAGTTACTTGAACGAGAGGTGAAC ATTCTGAAAAGTGTAAAACATGAACACATCATACATCTGGAACAAGTATTTGAAACGCCA AAGAAAATGTACCTTGTGATGGAGCTTTGTGAGGATGGAGAACTCAAAGAAATTCTGGAT AGGAAAGGCATTTCTCAGAGAATGAGACAAGGTGGATCATTCAAAGTCTCGCATCAGCT ATAGCATATCTTCACAATAATGATATTGTACATAGAGATCTGAAACTGGAAAATATAATG GTTAAAAGCAGTCTTATTGATGATAACAATGAAATAAACTTAAACATAAAGGTGACTGAT ACTCCTATCTATATGGCCCCTGAAGTTATCAGTGCCCACGACTATAGCCAGCAGTGTGAC ATTTGGAGCATAGGAGTCGTAATGTACATGTTATTACGTGGAGAACCACCCTTTTTGGCA AGCTCAGAAGCGAAGCTTTTTGAGTTAATAAGAAAAGGAGAACTACATTTTGAAAATGCA GTCTGGAATTCCATAAGTGACTGTGCTAAAAGTGTTTTGAAACAACTTATGAAAGTAGAT CCTGCTCACAGAATCACAGCTAAGGAACTACTAGATAACCAGTGGTTAACAGGCAATAAA CTTTCTTCGGTGAGACCAACCAATGTATTAGAGATGATGAAGGAATGGAAAAATAACCCA GAAAGTGTTGAGGAAAACACAACAGAAGAGAAGAATAAGCCGTCCACTGAAGAAAAGTTG AAAAGTTACCAACCCTGGGGAAATGTCCCTGAGACCAATTACACTTCAGATGAAGAGGAG GAAAAACAGTCTACTGCTTATGAAAAGCAATTTCCTGCAACCAGTAAGGACAACTTTGAT ATGTGCAGTTCAAGTTTCACATCTAGCAAACTCCTTCCAGCTGAAATCAAGGGAGAAATG GAGAAAACCCCTGTGACTCCAAGCCAAGGAACAGCAACCAAGTACCCTGCTAAATCCGGC GCCCTGTCCAGAACCAAAAAGAAACTCTAAGGTTCCCTCCAGTGTTGGACAGTACAAAAA CAAAGCTGCTCTTGTTAGCACTTTGATGAGGGGGTAGGAGGGGGAAGAAGACAGCCCTATG CTGAGCTTGTAGCCTTTTAGCTCCACAGAGCCCCGCCATGTGTTTGCACCAGCTTAAAAT TGAAGCTGCTTATCTCCAAAGCAGCATAAGCTGCACATGGCATTAAAGGACAGCCACCAG TAGGCTTGGCAGTGGGCTGCAGTGGAAATCAACTCAAGATGTACACGAAGGTTTTTTAGG GGGGCAGATACCTTCAATTTAAGGCTGTGGGCACACTTGCTCATTTTTACTTCAAATTCT TATGTTTAGGCACAGCTATTTATAGGGGAAAACAAGAGGCCAAATATAGTAATGGAGGTG CCAAATAATTATGTGCACTTTGCACTAGAAGACTTTGTTAGAAAATTACTAATAAACTTG CCATACGTATTACAGCAGAAGTGCTTCAGTCATTCACATGTGTTCGTGAGATTTTAGGTT GCTATAGATTGTTTAAGACAGCTTATTTTAAATGTAGAAAAATAGGAGATTTTGTAACTG CTTGCCATTAACTTGCTGCTAAATTCCCAATGTATTGATTAAATCAATAAAAAAACAGATG TTACTC

# FIGURE 2LL

CATGTGTGCAGGTTCATTGGCTGTGGCAGGAACGAGAAGTTTAACTATGTAGTGATGCAG AGCACCACATTGCGGCTGGGCAAGCAGATCTTGGAGTCCATCGAGGCCATCCACTCTGTG GGCTTCCTGCACCGTGACATCAAGCCTTCAAACTTTGCCATGGGCAGGCTGCCCTCCACC TACAGGAAGTGCTATATGCTGGACTTCGGGCTGGCCCGGCAGTACACCAACACCACGGGG GATGTGCGGCCCCTCGGAATGTGGCCGGGTTTCGAGGAACGGTTCGCTATGCCTCAGTC AATGCCCACAAGAACCGGGAGATGGGCCGCCACGACGACCTGTGGTCCCTCTTCTACATG CTGGTGGAGTTTGCAGTGGGCCAGCTGCCCTGGAGGAAGATCAAGGACAAGGAACAGGTA GGGATGATCAAGGAGAAGTATGAGCACCGGATGCTGCTGAAGCACATGCCGTCAGAGTTC CACCTCTTCCTGGACCACATTGCCAGCCTCGACTACTTCACCAAGCCCGACTACCAGTTG ATCATGTCAGTGTTTGAGAACAGCATGAAGGAGAGGGGCATTGCCGAGAATGAGGCCTTT GACTGGGAGAAGGCAGGCACCGATGCCCTCCTGTCCACGAGCACCTCTACCCCGCCCCCA GCAGAACACCCGGCAGACGGCAGCCATGTTTGGGGTGGTCAATGTGACGCCAGTGCCTGG GGACCTGCTCCGGGAGAACACCGCGGATGTGCTACAGGGAGAGCACCTGAGTGACCAGGA GAATGCACCCCAATTCTGCCCGGGAGGCCCTCTGAGGGGCTGGGCCACAGTCCCCACCT TGTCCCCCACCCGGGGGTCCTGAGGCTGAAGTCTGGGAGGAGACAGATGTCAACCGGAA TTTCTCTCACCCCGATTCCCAGCCTTGTGCCCCTGCCCTGTTCCTCCTAAGCACCCTGT CCCCGCCAATCTCCCTGCTTGCCCGGCCTCTGTTTCCGGTCCCCTCCCCGGCACTAGCC TCGCTGTGTCTTCCATCATCATCCTCTGTCTCCTTCACACTGAGGAGACCATCCGCC

SEO ID NO: 47 AA234451 H

GGCGCGCCAGATATCACACGTGCCAAGGGGCTGGCTCAGCGGCGGCGGCGGCAGGAGGGG GAGCAGGTGCTGGCACAAGAGCAGCGGCTTGGGGGAGCCGGCAGCAGCAGTAACAGCAGC AGCAGCCGCCGCCGCCGCCAGTAAACGCGGACCGTACCCCAGGGGACTACCCAGCCG GTGGCGGTCCCGCCGAGGGTTAACCCCCGCCGGTCCCGGTCCTGAGCTGGACCAGA GCCCTCCTCCAGAAACCCCTGCGTCCGCCACGGCCCAGGTTAAATGGAAACCACCCTTGG GAACTGGATGCCTGTGTAGCTGTTCTACCATATCAGTGTATTGCAATGAGTGGGGGAGGA GAGCAGCTGGATATCCTGAGTGTTGGAATCCTAGTGAAAGAAGATGGAAAGTGTTGAGA AAGATTGGGGGTGGGGGCTTTGGAGAAATTTACGATGCCTTGGACATGCTCACCAGGGAA AATGTTGCACTGAAGGTGGAATCAGCTCAACAACCAAAACAAGTTCTGAAAATGGAAGTT GCTGTTTTGAAAAAGCTGCAAGGGAAAGACCATGTTTGTAGATTTATTGGCTGTGGGAGG AATGATCGATTCAACTATGTGGTCATGCAGTTGCAGGGTCGGAATCTGGCAGATCTTCGC CGTAGCCAGTCCCGAGGCACATTCACCATTAGTACCACTCTCCGGCTGGGTAGACAGATT TTGGAGTCTATTGAAAGCATTCATTCTGTGGGATCTTGNCATCGAGACATCAAACCGTCG AACTTCGCTATGGGTCGCTTTCCTAGTACATGTAGGAAATGTTACATGCTTGATTTTGGC TTGGCTCGACAATTTACCAATTCCTGTGGTGACGTCAGACCACCTCGAGCTGTGGCAGGT TTTCGAGGGACAGTTCGTTATGCATCAATCAACGCACATCGGAACAGGGAAATGGGAAGA TGGAGAAAATAAAGGACAAGGAGCAAGTAGGCTCTATTAAGGAGAGATATGACCACAGG CTCATGTTGAAACATCTCCCTCCAGAATTCAGCATCTTTCTAGACCATATCTCTTTTTG GATTATTTTACAAAACCAGACTACCAGCTTCTTACATCCGTGTTTGACAATAGCATCAAG ACTTTTGGAGTAATTGAGAGTGACCCTTTTGACTGGGAGAAGACTGGAAATGATGGCTCC CTAACAACCACCACTACTTCTACCACCCCTCAGTTGCACACTCGCTTGACCCCTGCTGCA ATTGGAATTGCCAATGCTACTCCCATCCCTGGAGACTTGCTTCGAGAAAATACAGATGAG GTATTTCCAGATGAACAGCTTAGCGATGGAGAAAATGGCATCCCTGTTGGTGTCACCA GATAAATTGCCTGGATCTCTGGGACACCCCCGTCCCCAGGAGAAGGATGTTTGGGAAGAG

ATGGATGCCAACAAAACAAGATAAAGCTTGGAATTTGTAAGGCTGCTACTGAAGAGGAG AACAGCCATGGCCAGGCAAATGGTCTTCTCAATGCTCCAAGCCTTGGGTCACCAATTCGT

66/119

# FIGURE 2MM

SEQ ID NO: 48 AA435956 H  ${\tt ACTTTTACTATATTCTTTGAGATGACTGTTTTTGATTTAGAGGCGAAATCAGCACGTGGT}$ GGCTCAAATCTCCTTATGGATAGTGTTTCTTCCTTCCAGCTTTTCATGTTTCAACTTTTG CGGGGCCTGGCGTACATCCACCACCAACACGTTCTTCACAGGGACCTGAAACCTCAGAAC TTACTCATCAGTCACCTGGGAGAGCTCAAACTGGCTGATTTTGGTCTTGCCCGGGCCAAG TCCATTCCCAGCCAGACATACTCTTCAGAAGTCGTGACCCTCTGGTACCGGCCCCCTGAT GCTTTGCTGGGAGCCACTGAATATTCCTCTGAGCTGGACATATGGGGTGCAGGCTGCATC TTTATTGAAATGTTCCAGGGTCAACCTTTGTTTCCTGGGGTTTCCAACATCCTTGAACAG CTGGAGAAAATCTGGGAGGTGCTGGGAGTCCCTACAGAGGATACTTGGCCGGGAGTCTCC AAGCTACCTAACTACAATCCAGAATGGTTCCCACTGCCTACGCCTCGAAGCCTTCATGTT GTCTGGAACAGGCTGGGCAGGGTTCCTGAAGCTGAAGACCTGGCCTCCCAGATGCTAAAA GGCTTTCCCAGAGACCGCGTCTCCGCCCAGGAAGCACTTGTTCATGATTATTTCAGCGCC CTGCCATCTCAGCTGTACCAGCTTCCTGATGAGGAGTCTTTGTTTACAGTTTCAGGAGTG AGGCTAAAGCCAGAAATGTGTGACCTTTTGGCCTCCTACCAGAAAGGTCACCACCCAGCC CAGTTTAGCAAATGCTGGTGAAAAGAAAGGGCGAGATCACCAAGGTTCTTCCAGGGCTGT ATTTCTGCAGTTTCGGTTTTCATTTGCTTCAGCTTACTAAGAAGCTTCAAATCTAACTCC ATACTGAACAAGGGGCTTTATGTCCTCACCTATGACCTGGAATAGTTTAAATATGGTGTT CAAGGCAATAGTACATAATAGTGGAAGAAAATTCAGTGGAAGGTTATTGCTATTGTCATT TGCATAGAATTTAAGTGATTGATTTAAAAAAACTGGACATAAACTAAGTCTAAGAAG

SEQ ID NO: 49\_AA626859\_H

AAATGGAGTTGCTGATGGAGTGATCAAAAGCGTATTATGGCAAACACTTCAAGCTCTTAA

TTTCTGTCATATACATAACTGTATTCACAGAGATATAAAACCTGAAAATATTCTAATAAC

TAAGCAAGGAATAATCAAGATTTGTGACTTCGGGTTTGCACAAAATTCTGATTCCAGGAGA

TGCCTACACCGATTATGTAGCTACGAGATGGTACCGAGCTCCTGAACTTCTTGTGGGAGA

TACTCAGTATGGTTCTTCAGTCGATATATGGGCTATTGGTTGTGTTTTTTGCAGAGCTCCT

GACAGGCCAGCCACTGTGGCCTGGAAAATCAGATGTGGACCAACTTTATCTGATAATCAG

AACACTAGGAAAATTAATCCCAAGACATCAATCAATCTTTAAAAGTAACGGGTTTTTCCA

TGGCATCAGTATACCTGAGCCAGAAGACATGGAAACTCTTGAGGAAAAGTTCTCAGATGT

TCATCCTGTGGCTCTGAACTTCATGAAGGGGTGTCTGAAGATGAATCCAGATGAACAGATT

AACCTGTTCCCAACTCCTGGAGAGCTCCTACTTTGATTCTTTTCAAGAGGGCCCAAATTAA

AAGAAAAGCACGTAATGAAGGAAGAACAGAAGACCCCAACAGAATCAACTGTTGCCTCT

CATACCAGGAAGCCACATCTCCCCCCACACCTGATGGAAGAAAAAACAAGTCCTCCAGTTAAA

ATTTGATCACCTTCCAAACATTTAGGAAAAATGTTCTTTCAAGTGCAAATGAACTTTAATAT

GTACACATTTTGTACAAGTGAGGATAGGAATTCTCCAGTGTTTCAAATGCAAATGAGCCATA

WO 00/73469 PCT/US00/14842,

# FIGURE 2NN

 ${\tt TGAAAATTAAGATGCCTTCTAGAATTGGTTTGCTCTGATCATTGCTGATTCCTTTCCCCATGCTTTTACAT}$ 

SEQ ID NO: 50 AA061797 M

GAAAATAGCCCTGCGGGAAATCCGTATGCTGAAGTTGAAACACCCCAAACCTCGTGAACCT CATCGAGGTGTTCAGAAGAAGAAGAAGATGCATCTAGTTTTTGAGTACTGTGATCACAC ACTGTTAAACGAGCTGGAGAGAACCCAAACGGAGTTTCTGATGGAGTGATTAAAAGTGT GCTATGGCAAACCCTTCAAGCCCTTAACTTCTGTCACAAGCACAATTGTATTCATCGGGA TGTAAAACCTGAAAACATCCTAATAACCAAGCAAGGGATGATAAAGATTTGTGACTTTGG ATTTGCACGAATTCTAATTCCAGGAGACGCCTACACAGACTATGTTGCCACCAGGTGGTA CCGAGCCCCGAACTTCTCGTGGGAGACACGAAGTACGGTTCCTCTGTAGACGTGTGGGC CGTCGGCTGTGTTTTTGCAGAGCTCCTGACGGGTCAGCCACTCTGGCCGGGAAAATCCGA CGTGGACCAGCTTTACCTGATCATCAGGACGTTGGGGAAGCTGATTCCAAGACACCAGTC TATCTTTAGGAGTAACCAGTTTTTCCGCGGCATCAGCATACCTGAACCAGAGGACATGGA GACTCTTGAAGAAAATTCTCAAATGTTCAGCCTGTGGCTTTAAGTTTCATGAAGGGATG CCTGAAGATGAATCCTGATGAGAGGCTGACCTGTGCCCAGCTGCTGGACAGTGCCTACTT TGAGTCTTTTCAAGAGGATCAAATGAAAAGAAAAGCCCGCAGTGAGGGGGAGAAGCCGAAG GCGCCAGCAGAATCAACTGCTGCCTCTTATTCCTGGAAGCCACATCTCCCCCACACCTGA TGGAAGGAAACAAGTCGTCCAGTTAAAGTTCGATCATCTTCCAAACATTTAGGGGACTCA TCCTTCCCAGCACATCCTTTTAATATTGTCTACATAGGAATAAGACGGGAATCCTCAGCA TCTCAAATACAGTGAGCGACGTGAACACCAGGGCACCTCTAATCACCACGGGCTCCTCCC CTGTGCTTTTTCCACGCCAGCTCCATCTCCTAAAACATTCTCTTTAAATGTTGCAGTATC AAAATGGCACATCCGAAAGAGATGCTTCCAGTTTCACCAGAGCCGGGCTTCCTCAGGCAA TCGGTACTGTGCATCTGTGGACTTATGCTCCGACCTAGGGAAAGATTTCCACGTAGCCGT GGAGGGGATGGCCCTGAGCCCTCTCACTGGAGTTTCTTCTCCGTGCAGCCAGGTCTTACT TTAGACTACATTTGTGTTATTGTGGCATGGCAATCGTGAAAGGTGGTCTAGGTTTACCCT TGACTCCACAGCAGATGCTAGTCTCCTTCTCGTGAGGAGCTGACAAGTCTGCTTCTAAAA CGAACTAGAGAAAATTCCAAACGTGACCAGTTAGTGGACAGACTACAAGGAATCGACCAC CACCATGGTTTCTTTCTTTTTTTTTTTAATCTATTTGTACATATGAGAAAGAGGC AGAGGGGCGAGAGAAACCTCGTGTGTGAAAATCAAAAGACAAGCAGGAGGCCAGCCTAAG CTACATAGCAAGGCCTTTTCTCTACACCCATTCTCTAAGGTTGCTTAAACCCAAGTCCCT GCTGCTGATTGTATAAACTATGAATAAGTTCTACATATGTAGGACATATTGTTGTCATTG TTGAAATATCTAAGGATCTTGGTAGAAGCAGAAGTGTTCTAAATATTCTCCACACTGGTG AGTATCTTGGCATTTCATTTCTGACCTCATCACAGATGAACACATCAAAGGATGAGTATG TATCACTTTGCATCTTAGAATTCTACCTGTTTTAGCTGCGTTAAACCTTGTGAAAGGGCG GGGCCATAACTGAACCTGTGGAGTTCTTGCCTGTGTGCAGGAAACCCTCTGGTTTTGTCT CCAGCATGGAAGAAAACAGCTATAGTCACACCTACCTGAAAGTAGAAATTCAAAGTCACT GTCCTTGACTACATATGCAGTCCAAGGCCACGCTGGGCTACACTTCTCCAGGCATGAAGG TCCGTGTTTGTATCAAGGGCAGGAAAGGAGGTCCAAGGTCAAGGCCAGCCGAGGCTGC ATAGTGAGTTGAGGCTCTTCAGCAAAAGAAAGCAAACTAATAGGAGTCGTTGAAGGTAG CCACCGGCCATTTCTCTAAATATCATTCTGCTGAAAAGGGGGCTTAGTTTAGTTTAGAAT GCATTAATGTATGTAGAAGCTGGGCTATTTCAGATTATTTGAAATTGTAGCTATTGTTAA TTAGCACTTAATAACTAACTAGCATTATGGTAGTCTAAACTATTAGAGTTTACTACAAAG AGGTTTTGATTGAATTATATTAAACATATAATATGGATTTTAAAAATTTAAGATGTTTAA GAAAGCTATATAAAGATTAAACATTTTTGTGGCTGTATATTTGTGTATATACCTTGGTTG TTCTTTAAATTATTTTAATAAAAGCCAGAAACATT

# FIGURE 200

SEQ ID NO: 51 AA397553 H TTGCAGCCGTCATCGGGAGGCGGCAGCTCTAACAGCAGAGAGCGTCACCGCTTGGTATCG AAGCACAAGCGGCATAAGTCCAAACACTCCAAAGACATGGGGTTGGTGACCCCCGAAGCA GCATCCCTGGGCACAGTTATCAAACCTTTGGTGGAGTATGATGATATCAGCTCTGATTCC GACACCTTCTCCGATGACATGGCCTTCAAACTAGACCGAAGGGAGAACGACGACGTCGT GGATCAGATCGGAGCGACCGCCTGCACAAACATCGTCACCACCAGCACAGGCGTTCCCGG GACTTACTAAAAGCTAAACAGACCGAAAAAGAAAAAAGCCAAGAAGTCTCCAGCAAGTCG GGATCGATGAAGGACCGGATATCGGGAAGTTCAAAGCGTTCGAATGAGGAGACTGATGAC TATGGGAAGGCGCAGGTAGCCAAAAGCAGCAGCAAGGAATCCAGGTCATCCAAGCTCCAC AAGGAGAAGACCAGGAAAGAACGGGAGCTGAAGTCTGGGCACAAAGACCGGAGTAAAAGT CATCGAAAAAGGGAAACACCCAAAAGTTACAAAACAGTGGACAGCCCAAAACGGAGATCC AGGAGCCCCCACAGGAAGTGGTCTGACAGCTCCAAACAAGATGATAGCCCCTCGGGAGCT TCTTATGGCCAAGATTATGACCTTAGTCCCTCACGATCTCATACCTCGAGCAATTATGAC TCCTACAAGAAAAGTCCTGGAAGTACCTCGAGAAGGCAGTCGGTCAGTCCCCCTTACAAG GAGCCTTCGGCCTACCAGTCCAGCACCCGGTCACCGAGCCCCTACAGTAGGCGACAGAGA TCTGTCAGTCCCTATAGCAGGAGACGGTCGTCCAGCTACGAAAGAAGTGGCTCTTACAGC GGGCGATCGCCCAGTCCCTATGGTCGAAGGCGGTCCAGCAGCCCTTTCCTGAGCAAGCGG TCTCTGAGTCGGAGTCCACTCCCCAGTAGGAAATCCATGAAGTCCAGAAGTAGAAGTCCT GCATATTCAAGACATTCATCTTCTCATAGTAAAAAGAAGAGATCCAGTTCACGCAGTCGT CATTCCAGTATCTCACCTGTCAGGCTTCCACTTAATTCCAGTCTGGGAGCTGAACTCAGT AAGGGTTCACCTGTATTTTTGCCTAGAAAAGAGAACAGTTCAGTAGAGGCTAAGGATTCA GGTTTGGAGTCTAAAAAGTTACCCAGAAGTGTAAAATTGGAAAAATCTGCCCCAGATACT GAACTGGTGAATGTAACACATCTAAACACAGAGGTAAAAAATTCTTCAGATACAGGGAAA GTAAAGTTGGATGAGAACTCCGAGAAGCATCTTGTTAAAGATTTGAAAGCACAGGGAACA AGAGACTCTAAACCCATAGCACTGAAAGAGGAGATTGTTACTCCAAAGGAGACAGAAACA TCAGAAAAGGAGACCCCTCCACCTCTTCCCACAATTGCTTCTCCCCCACCCCCTCTACCA ACTACTACCCCTCCACCTCAGACACCCCCTTTGCCACCTTTGCCTCCAATACCAGCTCTT CCACAGCAACCACCTCTGCCTCCTTCTCAGCCAGCATTTAGTCAGGTTCCTGCTTCCAGT ACTTCAACTTTGCCCCCTTCTACTCACTCAAAGACATCTGCTGTGTCCTCTCAGGCAAAT TCTCAGCCCCCTGTACAGGTTTCTGTGAAGACTCAAGTATCTGTAACAGCTGCTATTCCA CACCTGAAAACTTCAACGTTGCCTCCTTTGCCCCTCCCACCCTTATTACCTGGAGGTGAT AGGACACGTCACTTACTCACAGACCTTCCTCTCCCTCCAGAGCTCCCTGGTGGAGĀTCTG TCTCCCCCAGACTCTCCAGAACCAAAGGCAATCACACCACCTCAGCAACCATATAAAAAG AGACCAAAAATTTGTTGTCCTCGTTATGGAGAAAGAAGACAAACAGAAAGCGACTGGGGG AAACGCTGTGTGGACAAGTTTGACATTATTGGGATTATTGGAGAAGGAACCTATGGCCAA GTATATAAAGCCAGGGACAAAGACACAGGAGAACTAGTGGCTCTGAAGAAGGTGAGACTA GACAATGAGAAAGAGGGCTTCCCAATCACAGCCATTCGTGAAATCAAAATCCTTCGTCAG TTAATCCACCGAAGTGTTGTTAACATGAAGGAAATTGTCACAGATAAACAAGATGCACTG GATTTCAAGAAGGACAAAGGTGCCTTTTACCTTGTATTTGAGTATATGGACCATGACTTA ATGGGACTGCTAGAATCTGGTTTGGTGCACTTTTCTGAGGACCATATCAAGTCGTTCATG AAACAGCTAATGGAAGGATTGGAATACTGTCACAAAAAGAATTTCCTGCATCGGGATATT AAGTGTTCTAACATTTTGCTGAATAACAGTGGGCAAATCAAACTAGCAGATTTTGGACTT TACCGACCTCCAGAACTACTGCTAGGAGAGGAACGTTACACACCAGCCATAGATGTTTGG AGCTGTGGATGTATTCTTGGGGAACTATTCACAAAGAAGCCTATTTTTCAAGCCAATCTG GAACTGGCTCAGCTAGAACTGATCAGCCGACTTTGTGGTAGCCCTTGTCCAGCTGTGTGG CCTGATGTTATCAAACTGCCCTACTTCAACACCATGAAACCGAAGAAGCAATATCGAAGG

# FIGURE 2PP

CGTCTACGAGAAGAATTCTCTTTCATTCCTTCTGCAGCACTTGATTTATTGGACCACATG CTGACACTAGATCCTAGTAAGCGGTGCACAGCTGAACAGACCCTACAGAGCGACTTCCTT AAAGATGTCGAACTCAGCAAAATGGCTCCTCCAGACCTCCCCCACTGGCAGGATTGCCAT GAGTTGTGGAGTAAGAAACGGCGACGTCAGCGACAAAGTGGTGTTGTAGTCGAAGAGCCA CCTCCATCCAAAACTTCTCGAAAAGAAACTACCTCAGGGACAAGTACTGAGCCTGTGAAG AACAGCAGCCCAGCACCACCTCAGCCTGCTCCTGGCAAGGTGGAGTCTGGGGCTGGGGAT GCAATAGGCCTTGCTGACATCACACACAGCTGAATCAAAGTGAATTGGCAGTGTTATTA AACCTGCTGCAGAGCCAAACCGACCTGAGCATCCCTCAAATGGCACAGCTGCTTAACATC CACTCCAACCCAGAGATGCAGCAGCAGCTGGAAGCCCTGAACCAATCCATCAGTGCCCTG ACGGAAGCTACTTCCCAGCAGCAGGACTCAGAGACCATGGCCCCAGAGGAGTCTTTGAAG GAAGCACCCTCTGCCCCAGTGATCCTGCCTTCAGCAGAACAGATGACCCTTGAAGCTTCA AGCACACCAGCTGACATGCAGAATATATTGGCAGTTCTCTTGAGTCAGCTGATGAAAACC CAAGAGCCAGCAGCAGTCTGGAGGAAAACAACAGTGACAAGAACAGTGGGCCACAGGGG CCCCGAAGAACTCCCACAATGCCACAGGAGGAGGCAGCATGTCCTCCTCACATTCTT CCACCAGAGAGAGGCCCCCTGAGCCCCCGGACCTCCACCGCCGCCACCTCCACCCCCT CTGGTTGAAGGCGATCTTTCCAGCGCCCCCAGGAGTTGAACCCAGCCGTGACAGCCGCC TTGCTGCAACTTTTATCCCAGCCTGAAGCAGAGCCTCCTGGCCACCTGCCACATGAGCAC CAGGCCTTGAGACCAATGGAGTACTCCACCCGACCCCGTCCAAACAGGACTTATGGAAAC ACTGATGGGCCTGAAACAGGGTTCAGTGCCATTGACACTGATGAACGAAACTCTGGTCCA GCCTTGACAGAATCCTTGGTCCAGACCCTGGTGAAGAACAGGACCTTCTCAGGCTCTCTG AGCCACCTTGGGGAGTCCAGCAGTTACCAGGGCACAGGGTCAGTGCAGTTTCCAGGGGAC CAGGACCTCCGTTTTGCCAGGGTCCCCTTAGCGTTACACCCGGTGGTCGGCCAACCATTC CTGAAGGCTGAGGGAAGCAGCAATTCTGTGGTACATGCAGAGACCAAATTGCAAAACTAT GGGGAGCTGGGGCCAGGAACCACTGGGGCCCAGCAGCTCAGGAGCAGGCCTTCACTGGGGG GGCCCAACTCAGTCTTCTGCTTATGGAAAACTCTATCGGGGGCCTACAAGAGTCCCACCA AGAGGGGAAGAGGAGAGGAGTTCCTTACTAA

# SEQ ID NO: 52 AA789239 H

TGAAAATGGAGATGTATGAAACCCTTGGAAAAGTGGGAGGGGAAGTTACGGAACAGTCA TGAAATGTAAACATAAGAATACTGGGCAGATAGTGGCCATTAAGATATTTTATGAGAGAC CAGAACAATCTGTCAACAAAATTGCGATGAGAGAAATAAAGTTTCTAAAGCAATTTCATC ACGAAAACCTGGTCAATCTGATTGAAGTTTTTTAGACAGAAAAAGAAAATTCATTTGGTAT TTGAATTTATTGACCACACAGTATTAGATGAGTTACAACATTATTGTCATGGACTAGAGA GTAAGCGACTTAGAAAATACCTCTTCCAGATCCTTCGAGCAATTGACTATCTTCACAGTA ATAATGTAATCATCCAGGGATATAAAACCTGAGAATATTTTAGTATCCCAGTCAGGAA TTACTAAGCTCTGTGATTTTGGTTTTGCACGAACACTAGCAGCTCCTGGGGACATTTATA CGGACTATGTGGCCACACGCTGGTATAGAGCTCCCGAATTAGTATTAAAAGATACTTCTT ATGGAAAGTATGTGCCTGTGGATATCTGGGCTTTTGGGCTGTATGATCATTGAGATGGCCA CTGGAAATCCCTATCTTCCTAGTAGTTCTGATTTGGATTTACTCCATAAAATTGTTTTGA AAGTGNGATTCATGCCAGAACTGAAAGCTAAATTACTGCAGGAAGCAAAAGTCAATTCAT TTTATACCAATACACTGCTAAGTAGTTCAGTTTTGGGAAAGGAAATAGAAAAAGAGAAAA AACCAAAAAGAAGAGTATGAAGGTGGACTTGGTCAACAGGATGCAAATGAAAATGTTC ATCCTATGTCTCCAGATACAAAACTTGTAACCATTGAACCACCAAACCCTATCAATCCCA GCACTAACTGTAATGGCTTGAAAGAAAATCCACATTGCGGAGGTTCTGTGACAATGCCAC CCATCAATCTAACTAACAGTAATTTGATGGCTGCAAATCTCAGTTCAAATCTCTTTCACC CCAGTGTGAGGTTAACTGAAAGAGCAAAAAAGAGACGCACTTCTTCACAATCTATTGGAC AAGTTATGCCTAATAGCAGGCAAGAGGATCCAGGTCCTATTCAAAGCCAAATGGAGAAGG GTATATTTAATGAGCGAACAGGTCACAGTGACCAAATGGCAAATGAGAACAAAAGGAAGC

70/113

# FIGURE 2QQ

SEQ ID NO: 53 AA124976 M  $\overline{\text{CTGGCAGATATAGTTCATGCTTGTTTACAAATTGATCCTGCTGAGAGGACATCATCTACT}$ GATCTTTTGCGTCACGATTACTTACTAGAGATGGATTTATTGAGAAATTCATACCAGAG CTGAGAGCTAAATTATTACAGGAAGCAAAGGTTAATTCATTTATAAAGCCAAAAGAGAAT TTTAAAGAAAATGAACCTGTGAGAGATGAGAAGAAATCAGTTTTTACCAACACCCTGCTC TATGGAAATCCATCACTTTATGGCAAGGAAGTGGACAGAGACAAAAGGGCCCAAGGAGCTC AAAGTCAGAGTCATTAAGGCCAAAGGGGGCAAAGGAGATGTCCCAGACCAGAAGAAGCCA GAGTATGAAGGCGACCACCGCCAGCAGGGCACAGCTGATGACACACAGCCCTCATCACTG GACAAGAAGCCTTCTGTCTTGGAACTGACAAACCCTCTCAATCCCAGTGAGAATTCTGAC GGTGTCAAAGAAGACCCACACGCTGGGGGTTGTATGATAATGCCACCTATCAACCTGACA AGCAGTAATTTGTTGGCCGCAAATCTCAGTTCAAACCTTTCCCACCCCAATTCACGGTTA ACTGAAAGAACAAAAAAGAGACGCACTTCTTCACAAACTATTGGACAGACTTTGTCTAAT AGCAGACAAGAGGACACAGGTCCCACACAAGTCCAAACAGAGAAAGGTGCATTTAATGAG TGCGACAGGAAAGAATTCCATTTCCCTGAACTGCCATTCACAGTGCAGGCGAAGGAGATG AAAGGGATGGAAGTTAAACAGATAAAAGTGCTGAAGAGAAATCAAAGAAAACAGATTCA TCTAAAATACCAACTTTACTTAGTATGGACCCAAATCAAGAAAAACAAGAGGGTGGAGAT ACTAGAATGTACATAGGTTGCTGCTAAGATAGCCACCCATCCCATCTGCATCAACATCAT CTATTTTTTTGGTTTTGCTAGCAAAATTTTCACAATTTTTCTCTATCTTCCAAAAACTGT CATGATTACTGAGTGGGTAGTCACATGATGTGCCCTGCTCGCACTGCTCTCAGACTGCTG AGACTCAAACCTCATAAGCCAGGGGTCTCCTGGGAAGCACTGGCCTCTTCAAGTGGATGC TCGATGAACCTTCTTATCTGTTGTCTTAGTAACCACTCGTTGCCATCACATGATGAAAGA CATTCTATTGTCCCCAGTGAAGCATTTATAGTACTTACATAACATGTTACAGTGATATGA TGTTCCTAGGTTAAACTCCTTGAGATGAAACTATTTCCTGCATTCTCTGACTCCCCTAGT CTAATAGTTCCTTCCATTTAGCCAGAAGAATTTCCTGAAGAAGCGATGCACAACCTGGGA AAGGTTTACTTTCTATCCTGGGCTGTTTTCTGTTGCTAAATAATATAGACTGGGTAGTTA **GTTAACAT** 

SEQ ID NO: 54\_AA575635\_M CCRK\_M
AGCGCCTCAGGCCAGCTCAAGATAGCTGACTTTGGCCTGGCCCGGGTCTTCTCTCCGGAT
GGTGGTCGCCTCTACACACATCAGGTGGCCACCAGGTGGTACCGAGCTCCTGAACTCCTG
TATGGCGCTCGGCAGTATGACCAGGGCGTTGACCTATGGGCTGTGGCTGCATCATGGGA
GAGCTGTTGAATGGGTCCCCCCTGTTCCCGGGCGAAAACGACATTGAACAACTGTGCTGT
GTGCTTCGCATCCTGGGTACCCCGAGTCCTCGAGTCTGGCCGGAGATCACAGAGCTGCCT
GACTACAACAAGATCTCCTTCGAGGAGCAGCACCAGTGCCCTTGGAGGAGGTGCTGCCT
GATGCCTCTCCCCCAGGCCTTGGACCTGCTGGGCCAGTTCCTCCTCCACGACAG

7/11/

WO 00/73469 PCT/US00/14842

### FIGURE 2RR

CATCCATCCGAGCTGCCAATTCCTCAGCGCCCAGGGGGACCTGCACCCAAGGCTCACCCA GGGCCCCCCATGTCCACGACTTCCATGTGGATCGACCTATTGAGGAGTCACTGTTGAAC CCAGAACTGATTCGGCCCTTCATCCCAGAGGGGTGAGATGCTGGTCCAGGCCTTCCTGCT CACCTGGTCCTGCTGGTGTGCTTGAGGGCTGGGCTCTGGGAGGCAGAACCGTGAGA TGTTCATCCCAGCAGAAAGAGACTCACGTCCTACAGACAAAGCCTCCAGAAACTGCTA GCTGTGTCCTCCAGGGCCACCCCTCAGTGGTGCCACCCGGCCTTAGAGATGATTGTC AGGCTCTGTCCCCTCTTCAAGGACATTGGTACTACAGCACCACCTGGTGGAAGCACAGAG TATAAGCTGTCTTCATACTGGGGACACAGCTGGGAAGTCAGACATGTTTTAGTTTTTGGTT CCACTGGGTCAGGATTTGAGGTTCATATAAAAGCCCTGGGTGTTTCTGTCTAATTGCACC TTGTCTGTTGCTGTTAGGGAAAGGACAATGGTGGGCCTTGATTCACAGGGGTCAGGTACT CAGAAGGGCCTCCTGTGAAGGCCATTTGGGTCCTCAGGCTTCCCATGCTATTCACGGGA CTTGAGTGCTCATTTGGGAGCGAGGGTCCAGAAGCTGAGGCCCAGGGATGGACAGTCCAG 

SEQ ID NO: 55\_AA631990\_H GAACAACAATAACAGAATAAGGAAG

GAACAACAATAACAGAATAAGGAAGAAAATCTCATGATTACCTCAATAAGTACAGAGAAA TCTGGTCACACTCACTATCCATTCATGATTACAACTCTTCAATACTATCGCGGCCGAGGA GGGAAGACGCCAGTTTGCCGACATTTCTCGGCCGAAGGGCCATTTGCTTTTGCGGAGATG CGGCATTCCAAAAGAACTCACTGTCCTGATTGGGATAGCAGAGAAAGCTGGGGACATGAA AGCTATCGTGGAAGTCACAAGCGGAAGAGGAGATCTCATAGTAGCACACAAGAGAACAGG CATTGTAAACCACATCACCAGTTTAAAGAATCTGATTGTCATTATTTAGAAGCAAGGTCC TTGAATGAGCGAGATTATCGGGACCGGAGATACGTTGACGAATACAGGAATGACTACTGT GAAGGATATGTTCCTAGACATTATCACAGAGACATTGAAAGCGGGTATCGAATCCACTGC AGTAAATCTTCAGTCCGCAGCAGGAGAAGCAGTCCTAAAAGGAAGCGCAATAGACACTGT TCAAGTCATCAGTCACGTTCGNATGAAATCGTGGACACTTTGGGTGAAGGAGCCTTTGGC AAAGTTGTAGAGTGCATTGATCATGGCATGGATGCATGTAGCAGTGAAAATCGTA AAAAATGTAGGCCGTTACCGTGAAGCAGCTCGTTCAGAAATCCAAGTATTAGAGCACTTA AATAGTACTGATCCCAATAGTGTCTTCCGATGTCCAGATGCTAGAATGGTTTGATCAT CATGGTCATGTTTGTATTGTGTTTGAACTACTGGGACTTAGTACTTACGATTTCATTAAA GAAAACAGCTTTCTGCCATTTCAAATTGACCACATCAGGCAGATGGCGTATCAGATCTGC CAGTCAATAAATTTTTTACATCATAATAAATTAACCCATACAGATCTGAAGCCTGAAAAT ATTTTGTTGTGAAGTCTGACTATGTAGTCAAATATAATTCTAAAATGAAACGTGATGAA CGCACACTGAAAAACACAGATATCAAAGTTGTTGACTTTGGAAGTGCAACGTATGATGAT GAACATCACAGTACTTTGGTGTCTACCCGGCACTACAGAGCTCCCGAGGTCATTTTGGCT TTAGGTTGGTCTCAGCCTTGTGATGTTTGGAGCATAGGTTGCATTCTTATTGAATATTAC CTTGGTTTCACAGTCTTTCAGACTCATGATAGTAAAGAGCACCTGGCAATGATGGAACGA ATATTAGGACCCATACCACAACACATGATTCAGAAAACAGAAAACGCAAGTATTTTCAC CATAACCAGCTAGATTGGGATGAACACAGTTCTGCTGGTAGATATGTTAGGAGACGCTGC AAACCGTTGAAGGAATTTATGCTTTGTCATGATGAAGAACATGAGAAACTGTTTGACCTG GTTCGAAGAATGTTAGAATATGATCCAACTCAAAGAATTACCTTGGATGAAGCATTGCAG CATCCTTTCTTTGACTTATTAAAAAAGAAATGAAATGGGAATCAGTGGTCTTACTATATA CTTCTCTAGAAGAGTTACTTAAGACTGTGTCAGTCAACTAAACATTCTAATATTTTTGT AAACATTAAATTATTTTGTACAGTTAAGTGTAAATATTGTATGTTTTGTATCAATAGCAT TCTTTTTGAAATTACCATTTTTAAATACCTTTGAAATATCCTTTGTGTCCAGTGATAAAT AGGAAATCTTGACTACTTTATATTCTTAAAGGAATATTCTTTATATACTTCAAATTTAGA

# FIGURE 2SS

ACTTAACTTTAAAAGTTTTTCTTCTGTAATTGTTGAACGGGTGATTATTATTAACTCTAG
ATAAGCAGGTACTAGAAACCAAAACTCAGAAAATGTTTACTGTTAGAATTCTATTAAATT
TTAAGTGTTGTATTCTTTTTCATTGGGTGATGTCAGGGTGATAACCAGACATTCATGGAA
AGGCATGCAGTTTGTCCATTGTGACAGTTTGTTTAATAAAACCACATACACACTTTATTT
AAGATTAAAATCTAACTGGAAAGTCAGCTTGGAAAATGGACATTTCCAAGTATGTTTGGT
GAGTCACAGATATAAAAATAGAAATTCTGATGAGAGGTTTCAGTTTTTAATACCAAGTCC
TTAGGAGTCTTAACATTGGCCAGCATCTGTTTATCAAATGACATAAATACGTAAACCTAT
AAGAATTAAGTTTATTAATTAGGCAATTTATGTCTGTGATAATTCTTACGGGAGAAAGAG
GATTTGATTGGAAAGCAGTTTGGGAAGAAAGTGCTGCTGAAATTTCCAGAATTTAATTGA
TTGGTTACATAAACTTTTTGACTTCAAT

SEQ ID NO: 56 AA557536 H AGTAAGGCCCCGCGGGCGTCCTGGCCGCCATGTGCACCGTAGTGGACCCTCGCATTGTCC GGAGATACCTACTCAGGCGGCAGCTCGGGCAGGGGAGAACATTCCGGGAAATCACGCTCC TCCAGGTGAGTGGCCTGGGCCCTCCAGTCCAATCCCCTTGCCCAGGTACAGATCTCTCCA GACAGGAGAGAAACTGGCCTTCTTGGGCCCCAGAGCACAGCCCCTCCTGGCCTTCCAGCC GCCTCCGACTCTCCCCAGGAGTTTGGGGGACCATCCCAACATCATCAGCCTCCTTGACG TGATCCGGGCAGAGAACGACAGGGACATTTACCTGGTGTTTGAGTTTATGGACACTGACC TGAACGCAGTCATCCGGAAGGGCGGCCTGCTGCAGGACGTCCACGTGCGCTCCATCTTCT ACCAGCTCCTGCGGGCCACCCGGTTCCTCCACTCGGGGCACGTTGTGCACCGGGACCAGA AGCCGTCCAATGTGCTCCTGGATGCCAACTGCACAGTGAAGCTGTGACTTTGGCCTGG CCCGCTCCCTGGGCGACCTCCCTGAGGGCCTGAGGACCAGGCCGTGACAGAGTACGTGG CCACACGCTGGTACCGAGCACCGGAGGTGCTGCTCTTCGCACCGCTACACCGCTTCCT GCCCCAGATACACCCTTGGGGTGGACATGTGGAGTCTGGGCTGTATCCTGGGGGAGATGC TGCGGGGGAGACCCCTGTTCCCCGGCACGTCCACCCTCCACCAGCTGGAGCTGATCCTGG AGACCATCCCACCGCCATCTGAGGAGXXXAGGCCACGACAGACGCTGGATGCCCTCCTAC CGCCAGACACCTCCCAGAGGCCTTGGACCTCCTTAGGCGACTCCTGGTGTTCGCCCCGG ACAAGCGGTTAAGCGCGACCCAGGCACTGCAGCACCCCTACGTGCAGAGGTTCCACTGCC CCAGCGACGAGTGGGCACGAGAGGCAGATGTGCGGCCCCGGGCACACGAAGGGGTCCAGC TCTCTGTGCCTGAGTACCGCAGCCGCGTCTATCAGATGATCCTGGAGTGTGGAGGCAGCA GCGGCACCTCGAGAGAGAGGGCCCGGAGGGTGTCTCCCCAAGCCAGGCACACCTGCACA AACCCAGAGCCGACCCTCAGCTGCCTTCTAGGACACCTGTGCAGGGTCCCAGACCCAGGC CCCAGAGCAGCCCAGGCCATGACCCTGCCGAGCACGAGTCCCCCCGTGCAGCCAAGAACG  ${\tt TTCCCAGGCAGAACTCCGCTCCCTGCTCCAAACTGCTCTCCTAGGGAATGGGGAAAGGC}$ CCCCTGGGGCGAAGCACCCCCCTTGACACTCTCGCTGGTGAAGCCAAGCGGGAGGG GAGCTGCGCCCTCCCTGACCTCCCAGGCTGCGGCTCAGGTGGCCAACCAGGCCCTGATCC GGCTTCCTCCGGAGGCCCGGCCCGGCCGGAGGATGTTCAGCACCTCTGCCTTGCAGGGTG CCCAGGGGGGTGCCAGGCTTTGCTTGGAGGCTACTCCCAAGCCTACGGGACTGTCTGCC ACTCGGCACTGGCCACCTGCCCTGCTGGAGGGGCACCATGTGTGAGCCGCCCTACTCC CTTCACCTGGCCCTCTGTTCCTGCCCCAGCNCCTTCCCCAGACCCCTCTCCAGTCTCCTG CACCCCTTAGCCCTGCTTTGCCTGGCCCGTTGAAGTTCCAGGGAGCTTGCCCGGGT CTCCTCGGGGGAGCAGATGAGGGCCCTGCCC

SEQ ID NO: 57\_N28606\_H, MOK\_H
ATGAAGACTATAAAGCAATTGGCAAAATAGGAGAGGGAACGTTTTCTGAAGTTATGAAG
ATGCAAAGCCTGAGAGATGGAAACTACTATGCATGTAAACAAATGAAGCAGCGCTTTGAA
AGTATTGAGCAAGTCAACAACCTACGAGAGATCCAAGCACTGAGGCGCCTGAATCCGCAC
CCAAACATTCTTATGTTGCATGAAGTGGTTTTTTGACAGAAAATCTGGTTCTCTTTGCACTA
ATATGTGAACTTATGGACATGAATATTTATGAGCTAATACGAGGGAGAAGATACCCATTA

#### FIGURE 2TT

TCAGAAAAAAAATTATGCACTATATGTACCAGTTATGTAAGTCCCTGGATCATATTCAC AGAAATGGAATATTTCACAGAGATGTAAAACCAGAAAATATACTAATAAAGCAGGATGTC CTGAAATTAGGGGACTTTGGCTCCTGCCGGAGTGTCTATTCCAAGCAGCCGTACACGGAA TACATCTCCACCGCTGGTACCGGGCCCCGGAGTGTCTCCTCACTGATGGGTTCTACACG TACAAGATGGACCTGTGGAGCGCCGGCTGTGTGTTCTACGAGATCGCCAGTCTGCAGCCC CTCTTTCCTGGAGTAAATGAACTGGACCAAATCTCAAAAATCCACGATGTCATCGGCACA CCCGCTCAGAAGATCCTCACCAAGTTCAAACAGTCGAGAGCTATGAATTTTGATTTTCCT TTTAAAAAGGGATCAGGAATACCTCTACTAACAACCAATTTGTCCCCACAATGCCTCTCC CTCCTGCACGCAATGGTGGCCTATGATCCCGATGAGAGAATCGCCGCCCACCAGGCCCTG CAGCACCCTACTTCCAAGAACAGAGGAAAACAGAGAAGCGGGCTCTGGGCAGCCACAGA AAAGCTGGCTTTCCGGAGCACCCTGTGGCACCGGAACCACTCAGTAACAGCTGCCAGATT TCCAAGGAGGCAGAAAGCAGAAACAGTCCCTAAAGCAAGAGGAGGACCGTCCCAAGAGA CGAGGACCGGCCTATGTCATGGAACTGCCCAAACTAAAGCTTTCGGGAGTGGTCAGACTG TCGTCTTACTCCAGCCCCACGCTGCAGTCCGTGCTTGGATCTGGAACAAATGGAAGAGTG CCGGTGCTGAGACCCTTGAAGTGCATCCCTGCGAGCAAGAAGACAGATCCGCAGAAGGAC CTTAAGCCTGCCCGCAGCAGTGTCGCCTGCCCACCATAGTGCGGAAAGGCGGAAGATAA

SEQ ID NO: 58 AB023153 H, ICK H ATGAATAGATACACAACAATCAGGCAGCTCGGGGATGGAACCTACGGTTCCGTCCTGCTG GGAAGAAGCATTGAGTCTGGGGAGCTGATCGCTATTAAAAAAATGAAAAGAAAATTTTAT TCCTGGGAGGAATGCATGAACCAACGGGAGGTTAAGTCTTTAAAGAAGCTCAACCATGCC AATGTAGTCAAATTAAAAGAAGTTATCAGGGAAAATGATCATCTTTATTTTATCTTCGAG TACATGAAGGAAAATCTTTACCAGCTCATTAAAGAGAGAAATAAGTTGTTTCCTGAGTCT GCTATAAGGAATATCATGTATCAGATATTACAAGGACTCGCATTTATTCACAAACTCGGC TTCTTTCATCGAGACTTAAAGCCTGAGAACCTCCTCTGCATGGGACCAGAACTTGTGAAA ATTGCAGACTTTGGTTTGGCCCGAGAAATACGATCAAAACCTCCATATACAGATTATGTA TCTACCAGATGGTACAGGGCTCCAGAAGTACTCCTGAGGTCTACCAACTACAGCTCCCCC ATTGACGTCTGGGCGGTGGGCTGCATCATGGCAGAAGTTTACACCCTCAGGCCACTCTTC CCTGGAGCCAGTGAAATTGACACAATATTCAAAATTTGCCAAGTGCTGGGGACACCAAAA AAGACTGACTGGCCTGAAGGCTATCAACTTTCAAGTGCAATGAACTTCCGTTGGCCACAG TGTGTACCCAATAACTTAAAGACCTTGATTCCCAATGCTAGCAGTGAAGCAGTCCAGCTC CTGAGAGACATGCTTCAGTGGGATCCCAAGAAACGACCAACAGCTAGTCAGGCACTTCGA TATCCTTACTTCCAAGTTGGACACCCACTAGGCAGCACCACAAAACCTTCAGGATTCA GAAAAACCACAGAAAGGCATCCTGGAAAGGGCAGGCCCACCTCCTTATATTAAGCCAGTC CCACCTGCCCAGCCAGCCAAGCCACACACACGAATTTCTTCACGACAGCATCAAGCC AGCCAGCCCCTCTGCATCTCACGTACCCCTACAAAGCAGAGGTCTCCAGGACAGATCAC CCAAGCCATCTCCAGGAGGACAAGCCAAGCCCGTTGCTTTTCCCATCCCTCCACAACAAG CATCCACAGTCGAAAATCACAGCTGGCCTGGAGCACAAAAATGGTGAGATAAAGCCAAAG AGTAGGAGAAGGTGGGGTCTTATTTCCAGGTCAACAAAGGATTCAGATGATTGGGCTGAC TTGGATGACTTGGATTTCAGTCCATCCCTCAGCAGGATTGACCTGAAAAACAAGAAAAGA CAGAGTGATGACACTCTCTGCAGGTTTTGAGAGTGTTTTTGGACCTGAAGCCCTCTGAGCCT GTGGGCACAGGAAACAGTGCCCCCACCCAGACGTCATATCAGCGGCGAGACACGCCCACC CTGAGATCTGCAGCCAAGCACTATTTGAAGCACTCTCGATACTTGCCTGGGATCAGT ATAAGAAATGGCATACTCTCGAATCCAGGCAAGGAATTTATTCCACCTAATCCATGGTCT AGTTCTGGCTTGTCTGGAAAATCTTCAGGGACAATGTCAGTAATCAGCAAAGTAAATTCA AAAAAAGAAATCGGTTCTGCTATGCAGAGGGTACACCTAGCACCTATTCCAGACCCTTCC CCTGGTTATTCCTCCCTGAAGGCCATGAGACCTCATCCTGGGCGACCATTCTTGGACACC CGGACAGACTGGGCTTCCAAGTACCCATCCCGGCGGTGA

### FIGURE 2UU

SEQ ID NO: 59 AA839940 M AGCAGCAACAATGGTGGCATGAGTGCAGAGGAGGAGATAGGGCCTGGGGCTGAGCCTATG AGAGGACCAAGCTTGGCTACAAGGGACTGGAGAGATGAGACTGTTGGGACCACAGACCTG CAGCAAGGCATAGACCCAGGAGCAGTGAGCCCTGAGCCTGGGAAGGACCACGCAGCCCAG GGCCCAGGAAGAACTGAAGCTGGAAGGGTATCTTCTGCTGCAGAGGCTGCCATTGTGGTT CTAGATGACAGCGCAGCCCCCAGCCCCTTTTGAACACCGGGTAGTGAGCATCAAAGAT ACCCTGATCTCAGCAGGCTACACGGTATCCCAACATGAAGTCTTAGGAGGGGGTCGGTTT GGCCAGGTGCACAGGTGTACAGAGAGGTCTACAGGCCTTGCACTGGCAGCCAAGATCATC AAAGTGAAGAACGTAAAGGACCGGGAGGATGTGAAGAATGAGGTCAACATCATGAACCAG CTCAGCCACGTAAACTTGATCCAACTTTATGATGCGTTTGAGAGCAAGAACAGCTTCACT CTGATCATGGAGTATGTGGATGGAGGCGAACTCTTTGACCGGATCACGGATGAGAAGTAC CACCTCACTGAGTTGGATGTGGTCTTGTTCACGAGGCAGATCTGTGAGGGTGTGCATTAC CTGCATCAGCACTATATCCTGCACCTGGACCTCAAGCCTGAGAACATATTGTGTGTCAGC GAGAAGCTAAAGGTGAACTTTGGTACTCCGGAGTTCCTGGCCCCAGAAGTTGTTAACTAT GAGTTTGTGTCATTTCCAACAGACATGTGGAGTGTGGGAGTTATCACCTACATGCTACTC AGTGGTTTGTCCCCATTTCTAGGGGAGACAGATGCAGAGACCATGAATTTTATTGTGAAC TGCAGCTGGGATTTCGATGCTGATACCTTCAAAGGGCTGTCGGAGGAAGCCAAGGACTTT GTTTCCCGGTTACTGGTCAAAGAGAGAGCTGTAGGATGAGCGCCACACAGTGCCTGAAA CACGAGTGGTTAAATCACCTGCCTGCCAAAGCCTCGGGCTCCAACGTTCGCCTCAGATCC CAACAACTGCTGCAGAAATATATGGCTCAGAGTAAATGGAAGAAACATTTCCACGTĞGTG GCTGCAGTCAACAGGCTACGGAAATTTCCAACGTGTCCCTAATCTTCAACTCTGGTGTTC CACTGGGCCTGGGAATTCTTGAGGCAACACGAAGTGGTAATATGAAGAGATTACTCAAGA TTTTATGTAGATTGGCGCTTTGCTATTATTGATTTTTCTTATTTTGCAAAGAATGATGGA AGGAAGCAAGAAAGAAAGAAAGAAAAGGGGGGAAGAAAAGGAAAAGGCAGAAAGCAA GGAAACAGGCTACGTTGTTGCTCTTCTTGTAGGTGAAAGTGTTTTTATTAAAAGCCCTAG TTCCTTTTGGTAATAAGAGCAGGCACGCTCAGGATGGGCAGGGAAATCCTACTTGGCTTT GAAGAGGGAGGAATTAGGTCCAACAGTGGGGGATGAATTTGACCGAAACATTGTATAAAA TTCTTAAAGAATTAATAAAATATATTTTTAAAGGAG

SEQ ID NO: 60 AA460132 H GGAACCTCAGGCTTCAGAGAGCCGAAAAGTTGGGAGGCGTAACCACTTACAGGCCGGAAG TGTCCGGGGTGGACGCATTCGGGTAGCCGAAGAAGTCCCAGGATTGCCGAAGAAGTCCCA GGATTTCCGAAGCGAGCCGAAGCATCGCGACAGTTTTCAGAGACAGCTGATCGGTTGGAG CCCGCCCGGAGGCTGAGGCTCTGGCCGCAGCCCGGGAGCGGAGCAGCCGCTTCTTGAGC GGCCTGGAGCTGGTGAAGCAGGGTGCCGAGGCGCGCGTGTTCCGTGGCCGCTTCCAGGGC CGCGCGGCGTGATCAAGCACCGCTTCCCCAAGGGCTACCGGCACCCGGCGCTGGAGGCG CGGCTTGGCAGACGGCGGACGGTGCAGGAGGCCCGGGCGCTCCTCCGCTGTCGCCGCGCT GGAATATCTGCCCCAGTTGTCTTTTTTGTGGACTATGCTTCCAACTGCTTATATATGGAA GAAATTGAAGGCTCAGTGACTGTTCGAGATTATATTCAGTCCACTATGGAGACTGAAAAA ACTCCCCAGGGTCTCTCCAACTTAGCCAAGACAATTGGGCAGGTTTTGGCTCGAATGCAC GATGAAGACCTCATTCATGGTGATCTCACCACCTCCAACATGCTCCTGAAACCCCCCCTG GAACAGCTGAACATTGTGCTCATAGACTTTGGGCTGAGTTTCATTTCAGCACTTCCAGAG GATAAGGGAGTAGACCTCTATGTCCTGGAGAAGGCCTTCCTCAGTACCCCATCCCAACACT GAAACTGTGTTTGAAGCCTTTCTGAAGAGCTACTCCACCTCCTCCAAAAAGGCCAGGCCA AAGAATGTGTATGACAACCACACACAGTGAAGCTCTTTTTTCAAAGTAAATTTGAAGAAA

#### FIGURE 2VV

SEQ ID NO: 61 SGK034 H CAGAGAGAGAAGGTAAACCAAGGGAACATGCCAGGGCTTCAGAGCACCTTCCTAGCCATG GACACGGAGGAGGGGTAGAGGTGTGTGGAACGAGCTCCACTTCGGAGACAGGAAGGCC TTCGCGGCGCACGAGGAGAAGATCCAGACCGTGTTCGAGCAGCTGGTGCTGGTGGACCAC CCGAACATCGTGAAGTTGCACAAGTACTGGCTGGATACCTCTGAGGCCTGCGCGAGGGTC ATCTTCATCACAGAGTACGTGTCATCAGGCAGCCTCAAGCAATTCCTCAAAAAGACCAAG AAGAACCACAAGGCCATGAACGCCCGGGCCTGGAAGCGCTGGTGCACGCAGATCCTGTCT GCGCTCAGCTTCCTGCACGCCTGCAGCCCCCCAATCATCCACGGGAACCTGACCAGCGAC ACCATCTTCATTCAGCACAACGGCCTCATCAAGATCGGCTCCGTGTGGCACCGAATCTTC TCCAATGCACTTCCAGATGATCTCCGAAGCCCCATCCGCGCTGAGCGAGAGGAACTTCGG AACCTGCACTTCTTCCCCCCAGAGTATGGAGAGGTGGCCGATGGGACCGCTGTGGACATC TTCTCCTTTGGGATGTGTGCGCTGGAGATGGCTGTACTGGAAATCCAGACCAATGGGGAC ACCCGGGTCACAGAGGAGGCCATTGCTCGCGCCAGGCACTCGCTGAGTGACCCCAACATG CGGGAGTTCATCCTTTGCTGCCTGGCCCGGGACCCTGCCCGGCCCTCTGCCCACAGC CTCCTCTTCCACCGCGTGCTCTTCGAGGTGCACTCGCTGAAGCTCCTGGCAGCCCACTGC TTCATCCAGCACCAGTACCTCATGCCTGAGAATGTGGTGGAGGAGAAGACCAAGGCCATG GACCTGCACGCGGTCTTGGCGGAGCTTCCCCGGCCCCGCAGGCCCCCGCTGCAGTGGCGG TACTCGGAAGTCTCCTTCATGGAGCTGGACAAATTCCTGGAGGATGTCAGGAATGGAATC TACCCACTGATGAACTTTGCAGCCACTCGACCCCTGGGGCTGCCCCGTGTGCTGCCCCA CCCCGGAGGAGGTCCAAAAGGCCAAGACCCCGACGCCAGAGCCCTTTGACTCTGAGACC AGAAAGGTCATCCAGATGCAGTGCAACCTGGAGAGAGGGGGGACAAGGCGCGCTGGCAT CTCACTCTGCTTCTGGTGCTGGAAGACCGGCTGCACCGGCAGCTGACCTACGACCTGCTC CCAACGGACAGCGCCCAGGACCTCGCCTCGGAGCTCGTGCACTATGGCTTCCTCCACGAG GACGACCGGATGAAGCTGGCCGCCTTCCTGGAGAGCACCTTCCTCAAGTACCGTGGGACC CAGGCCTGACCCGGAGCCCCAGCCCCAGGGGACCATGCCGGGGTGCTGCCCGGGCAGGCC ATGTTGGGGAGACTCCAGCACCGTGGGGCTGCCCTCCTCCATGCGCCTGGGAGCACAAAG GCCCGGTAGTGAAGGAACCCCCGTCTCCTGAGAGTGGGGCTGACCCTGCCTTGGGCGC CGAGGGGTTGGGGGTGTGGGGGAGCCGTTAGGCCTCCCAGGTCCTTAGGATCAGG GTTGCCCCCAGAACCCCTTCCCATATCCTCCATTCTCCGCCCTGAGTTCCTACCCAGGCT GCCTGGCTGGGGCCACTGCCTCCTCAGCATGCAGGAGGCTGCCCTGTAGGGAACCCCAGC TCTGGGGCTTGGGGGTGAGGGTCAGCCCTGGACAGACCTCTGCCCAGGGAACTGCTCCAT GGGGTCTGGGAGAGCAGCCATCCCCTGCTGGCACCATAGACCCACACAAGGAGCCTGCAC AGCAAGCCAGCGGTGACACCCTGCAGGTGTCAGGCATGGCACTGGGCACAACAGGGACC TGGCAGGAGAAACAGACCACAGAGAGGTCTGGAGTTGAGGCTGTTGTCAGCAAAGCCCCT AACTTGCAGCCCCTCTGCAGATCTCCTCTGGCCACTGCAGCCCCTCCAATGGGCTTTTTC TCTCATGCATTCCCTGGCCTGGAGGCGTCAGGGACCCCACATCCTCCCTGCTCCTCAGAC TCACAGCCCCTCCATGTTACCTCCCGCACCTCCTCCCTGGGGCAGCTGCTCCCTGGGCCT CTGAGGATGTCAGCTCCTGGCTCCCTGCCTCTCTCCCACTCCACTCCTGGCTCAGTCTTA GAGATTTCTATGCCCTCATGGATTCTACCCCTGCCTTCCTGGCCTCTTGATTCTTGGCTT GCCTCTCCAATTCCAAACTTAGTGAAATGGCCTTAAGCATTTTAAACTGTATATA CATTAGCGCATTCATGCCTTTCTAAACGCATTTCAAATGTCAACCAGGAAGGCACACCAC

# **FIGURE 2WW**

SEQ ID NO: 62 AA103218 M SGK034 M  $\overline{\texttt{CCACGCGTCCGCACCAGAGTATGGCGAAGTCAATGATGGGACTGGCTTTGTGGACATCTT}$ CTCCTTCGGGATGTGTGCACTGGAGATGGCTGTACTCGAGATCCAAGCCAACGGGGATAC GGAATTCATCCTCTCCTGCCTGGCCCGGGACCCTGCCCGACCCTCAGCCCACAACCT CCTCTTCCACCGAGTGCTCTTTGAGGTGCACTCGCTGAAGCTGCTGGCAGCTCACTGCTT CATCCAGCACCAGTACCTCATGCCTGAGAATGTGGTAGAGGAAAAGACCAAGGCCATGGA CCTCCATGCAGTTTTGGCTGAGATGCCGCAGCCCCATGGACCCCCAATGCAGTGGCGGTA CTCAGAGGTCTCCTTCTTGGAGCTGGACAAATTCCTAGAGGATGTCAGGAACGGGATGTA TCCACTGATGAACTTTGCGGCTGCTCGGCCCTTGGGGCTTCCCCGTGTGTTGGCCCCACC CCCAGAGGAAGCCCAAAAGGCCAAAACTCCAACGCCAGAACCCTTTGACTCGGAGACCAG GAAGGTGGTCCAGATGCAGTGCAACCTGGAAAGAAGCGAGGACAAGGCTCGGTGGCACCT TACTCTGCTCTTGGTGCTTGAGGACCGGCTACATCGGCAGCTGACCTATGATCTGCTCCC AACGGACAGTGCCCAGGACCTCGCTGCTGAACTAGTGCATTATGGCTTCCTGCACGAGGA TGACAGGACAAAGCTAGCAGCCTTTCTGGAGACCACTTTTCTCAAGTACCGAGGGACGCA AGCGTGACCTTCCCAGTCCTGACGGCCCAGCAGAGATACAGGGGCTCAGGGTTGTCCACT TGGCAAAGAGCCCCCACACTGCTCAAAGCTGCCTTCTGCCTGTGTTCCCTGGAACTGAAC ACAGGCCCTGCTAGTGAAGACACCCCCACCCCCAGCTTTCTGCAGCAGTGTGGGACCCT GGGGTGGTGATGGAGCCTGAGCCTGGACGAGAGTGGATACAGGTCAGTTAGGGGAACCG CTCCATCTGGTACTAGACAACAGCCATGCCTTCAGGTGGCATAGAAACCTAGGGAAGGAG CCTGAACTCAGGTGTCACAGTGCTGGGCATCAGGCAGACCAGACCTGACCTGATTGGAGA ACTGTAGACTAGATAGCTTGGAGTTGAACCCATGGCCAGGGAATTCCTTGGTCCTCA GACCAGTCCTGATCCCTTGCAGACCTGCCTTGAGCCCTCTTTCTGATCTTCCACACTCTT GAGACCAGGACCTGTGTCCTCCCCAAAGCCCTTGGGAAGGATCTTTCTATTCATCATCCC GTTTGAGTTGAGGATGTGGGTTCCTGGCTCCCTCTTTCTCCCCAGCCCAACTTGTCTCTT TCTTACTGGTTTCAAAGTCCTGATGAACGCTTCCCCTCAGAGCCACCCTGGTTTCCTTGG TTCTTGAACTGCCTCTCCCCAACTTCAAACCAGGTCTTAAACGTTTTTTAAATGCATAT ATAAATGTAATGCAGTCACGGTCCTTTTTAAACACTTTGTGTATGAAACCAGGAAAGCTC ACTATTGTATTAGGAATAGTTCCACATTGCTGCTGTTAACAGATATCATAAACCCAGTGG CATCAAGTGTGATCCAGGCTCTCACTAGATTAATACCCAGGCTAAGTTCCTTTCTGGAAG CTGGGACTTACCTCCTGCTCCTTCAAGCTATTGGCAGAACTCACTTCCCTGCAATGGTAA GGCAGAAATCCCTATTTTCTCAACAGCTGCCAACTAAGAACCCCTCTCAGCTTCTAGAGG

### FIGURE 2XX

CCACCAACTTTTCTTAGTTCTTCTTCTCCCCCCTCAAGACCAGCAGCGTCAAGTTGAAT CTTTGTCCTGGGCTAGCTGACTGGCTTGCCACTGCTGGGAAGAGTTGGGGCCTTTTGTGA GTAGGTTGGACCCACCAGGATAACCGAGGATGATCCCCTTCTCAGGGTCTATAGATGAAC CACACCTGCGCAGTTCCTTCTGCTGTCATCCTGGGCTTTGGTGCTTGGAGAACAGCCGTG GGCGGTGGGTGTTGTTACTGTGGTACCTACCATGCCATCTTAACCGAAACCAAGACCTAA AATAAAACAGATTTGTCATGGGACATCTAATAAATTAAATGAACTCTG

SEQ ID NO: 63 NEK7 H, N34132 H CACGAATCCGAGCCCGCTCGCCTCTCTCCAGCGAACCGACCATGTCTGGCGGCGCCGCAG AGAAGCAGAGCACTCCCGGTTCCCTGTTCCTCTCGCCGCCGGCTCCTGCCCCCAAGA ACGGCTCCAGCTCCGATTCCTCCGTGGGGGAGAAACTGGGAGCCGCGGCCGCCGACGCTG TGACCGCCAGGACCGAGGAGTACAGGCCGCCGCCACACTATGGACAAGGACAGCCGTG GGGCGGCCGCGACCACCACCACTGAGCACCGCTTCTTCCGCCGGAGCGTCATCTGCG ACTCCAATGCCACTGCACTGGAGCTTCCCGGCCTTCCTCTTTCCCTGCCCCAGCCCAGCA TCCCCGCGGCTGTCCCGCAGAGTGCTCCACCGGAGCCCCACCGGGAAGAGACCGTGACCG CCACCGCCACTTCCCAGGTAGCCCAGCAGCCTCCAGCCGCTGCCGCCCCTGGGGAACAGG CCGTCGCGGGCCCTCGACTGTCCCCAGCAGTACCAGCAAAGACCGCCCAGTGT CCCAGCCTAGCCTTGTGGGGAGCAAAGAGGGGCCGCCGCCGCGGCGAGAAGTGGCAGCGGCG TGGAGACCAAGGCCGTGGGAATGTCTAACGATGGCCGCTTTCTCAAGTTTGACATCGAAA TCGGCAGAGGCTCCTTTAAGACGGTCTACAAAGGTCTGGACACTGAAACCACCGTGGAAG TCGCCTGGTGTGAACTGCAGGATCGAAAATTAACAAAGTCTGAGAGGCCAGAGATTTAAAG AAGAAGCTGAAATGTTAAAAAGGTCTTCAGCATCCCAATATTGTTAGATTTTATGATTCCT GGGAATCCACAGTAAAAGGAAAGAAGTGCATTGTTTTGGTGACTGAACTTATGACGTCTG GAACACTTAAAACGTATCTGAAAAGGTTTAAAGTGATGAAGATCAAAGTTCTAAGAAGCT GGTGCCGTCAGATCCTTAAAGGTCTTCAGTTTCTTCATACTCGAACTCCACTTATCATTC ACCGCGATCTTAAATGTGACAACATCTTTATCACCGGCCCTACTGGCTCAGTCAAGATTG GAGACCTCGGTCTGGCAACCCTGAAGCGGGCTTCTTTTGCCAAGAGTGTGATAGGTACCC CAGAGTTCATGGCCCCTGAGATGTATGAGGAGAAATATGATGAATCCGTTGACGTTTATG CTTTTGGGATGTGCATGCTTGAGATGGCTACATCTGAATATCCTTACTCGGAGTGCCAAA TAGCAATTCCTGAAGTGAAGGAAATTATTGAAGGATGCATACGACAAAACAAAGATGAAA GATATTCCATCAAAGACCTTTTGAACCATGCCTTCTTCCAAGAGGAAACAGGAGTACGGG TAGAATTAGCAGAAGAAGATGATGGAGAAAAAATAGCCATAAAATTATGGCTACGTATTG AAGATATTAAGAAATTAAAGGGAAAATACAAAGATAATGAAGCTATTGAGTTTTGTTTTG ATTTAGAGAGAGATGTCCCAGAAGATGTTGCACAAGAAATGGTAGAGTCTGGGTATGTCT GGAAACGAGAGCAGCGGCAGTTGGTACGGGAGGAGCAAGAAAACAAAAAGCAGGAAGAGA GCAGTCTCAAACAGCAGGTAGAACAATCCAGTGCTTCCCAGACAGGAATCAAGCAGCTCC CTTCTGCTAGCACCGGCATACCTACTGCTTCTACCACTTCAGCTTCAGTTTCTACACAAG TAGAACCTGAAGAACCTGAGGCAGATCAACATCAACAACTACAGTACCAGCAACCCAGTA TATCTGTGTTATCTGATGGGACGGTTGACAGTGGTCAGGGATCCTCTGTCTTCACAGAAT CTCGAGTGAGCAGCCAACAGACAGTTTCATATGGGTTCCCAANNCATGAACAGGCACATT CTACAGGCACAGTCCCAGGCCATATACCTTCTACTGTCCAAGCACAGTCTCAGCCCCATG GGGTATATCCACCCTCAAGTGTGCAGCAGGGAATACAGCAGACAGCCCCTCCTCAACAGA CAGTGCAGTATTCACTTTCACAGACATCAACCTCCAGTGAGGCCACTACTGCACAGCCAG TGAGTCAGCCTCAAGCTCCACAAGTCTTGCCTCAAGTATCAGCTGGAAAACAGAGTACTC AGGGAGTCTCTCAGGTTGCTCCTGCAGAGCCAGTTGCAGTAGCACAGCCCCAAGCTACCC AGCCGACCACTTTGGCTTCCTCTGTAGACAGTGCACATTCAGATGTTGCTTCAGGTATGA 

# FIGURE 2YY

GGCATTACCGAAAATCTGTAAGGAGTCGCTCTCGACATGAAAAACTTCACGCCCAAAAT TAAGAATTTTGAATGTTTCAAATAAAGGAGACCGAGTAGTAGAATGTCAATTAGAGACTC ATAATAGGAAAATGGTTACATTCAAATTTGACCTAGATGGTGACAACCCCGAGGAGATAG AAGTGCGAGAAATTATTGAAAAAGCTGATGAAATGCTCAGTGAGGATGTCAGTGTGGAAC CAGAGGGTGATCAGGGATTGGAGAGGTCTACAAGGAAAGGATGACTATGGCTTTTCAGGTT CTCAGAAATTGGAAGGAGAGTTCAAACAACCAATTCCTGCGTCTTCCATGCCACAGCAAA TAGGCATTCCTACCAGTTCTTTAACTCAAGTTGTTCATTCTGCGGGAAGGCGGTTTATAG TGAGTCCTGTGCCAGAAAGCCGATTACGAGAATCAAAAGTTTTCCCCAGTGAAATAACAG ATACAGTTGCTGCCTCTACAGCTCAGAGCCCTGGAATGAACTTGTCTCACTCTGCATCAT CCCTTAGTCTACAACAGGCCTTTTCTGAACTTAGACGTGCCCAAATGACAGAAGGACCCA ATACAGCACCTCCAAACTTTAGTCATACAGGACCAACATTTCCAGTAGTACCTCCTTTCT TAAGTAGCATTGCTGGAGTCCCAACCACAGCAGCAGCACCAGCACCAGTCCCTGCAACAA GCAGCCCTCCTAATGACATTTCCACATCAGTAATTCAGTCTGAGGTTACAGTGCCCACTG AAGAGGGGATTGCTGGAGTTGCCACCAGCACAGGTGTGGTAACTTCAGGTGGTCTCCCCA TACCACCTGTGTCTGAATCACCAGTACTTTCCAGCGTAGTTTCAAGTATCACAATACCTG CAGTTGTCTCAATATCTACTACATCCCCGTCACTTCAAGTCCCCACATCCACATCTGAGA TCGTTGTTTCTAGTACAGCACTGTATCCTTCAGTAACAGTTTCAGCAACTTCAGCCTCTG CAGGCAGCACTACTGTGGGAGCCACATTAACATCAGTTTCTACCACCACTTCATTCCCAA GCACAGCTTCACAGCTGTCCATTCAGCTTAGCAGCAGTACTTCTACTCCTACTTTAGCTG AAACCGTGGTAGTTAGCGCACACTCACTAGATAAGACATCTCATAGCAGTACAACTGGAT TGGCTTTCTCCCTCTGCACCATCTTCCTCTTCCTCTGGAGCAGGAGTGTCTAGTT ATATTTCTCAGCCTGGTGGGCTGCATCCTTTGGTCATTCCATCAGTGATAGCTTCTACTC CTATTCTTCCCCAAGCAGCAGGACCTACTTCTACACCTTTATTACCCCAAGTACCTAGTA TCCCACCCTTGGTACAGCCTGTTGCCAATGTGCCTGCTGTACAGCAGACACTAATTCATA GTCAGCCTCAACCAGCTTTGCTTCCCAACCAGCCCCATACTCATTGTCCTGAAGTAGATŢ CTGATACACAACCCAAAGCTCCTGGAATTGATGACATAAAGACTCTAGAAGAAAAGCTGC GGTCTCTGTTCAGTGAACACAGCTCATCTGGAGCTCAGCATGCCTCTGTCTCACTGGAGA CCTCACTAGTCATAGAGAGCACTGTCACACCAGGCATCCCAACTACTGCTGTTGCACCAA CAGTTGCTTTGCCAGTTACACCAGTGGTCACACCTGGGCAAGTTTCTACCCCAGTCAGCA CGGTGCTGCCAGTGGGTACTGAACTTCCAGCAGGTACTCTACCCAGCGAGCAGCTGCCAC CTTTTCCAGGACCTTCTCTAACCCAGTCCCAGCAACCTCTAGAGGATCTTGATGCTCAAT TGAGAAGAACACTTAGTCCAGAGATGATCACAGTGACTTCTGCGGTTGGTCCTGTGTCCA TGGCGGCTCCAACAGCAATCACAGAAGCAGGAACACAGCCTCAGAAGGGTGTTTCTCAAG TCAAAGAAGGCCCTGTCCTAGCAACTAGTTCAGGAGCTGGTGTTTTTAAGATGGGACGAT TTCAGGTTTCTGTTGCAGCAGACGGTGCCCAGAAAGAGGGGTAAAAATAAGTCAGAAGATG CAAAGTCTGTTCATTTTGAATCCAGCACCTCAGAGTCCTCAGTGCTATCAAGTAGTAGTC CAGAGAGTACCTTGGTGAAACCAGAGCCGAATGGCATAACCATCCCTGGTATCTCTTCAG ATGTGCCAGAGAGTGCCCACAAAACTACTGCCTCAGAGGCAAAGTCAGACACTGGGCAGC CTACCAAGGTTGGACGTTTTCAGGTGACAACTACAGCAAACAAGTGGGTCGTTTCTCTG AACTGTCAGAGCCTTCACATCTAAATGGGCCGTCTTCTGACCCGGAGGCCGCTTTTTTAA GTAGGGATGTGGATGGTTCCGGTAGTCCACACTCGCCCCATCAGCTGAGCTCAAAGA GCCTTCCTAGCCAGAATCTAAGTCAAAGCCTTAGTAATTCATTTAACTCCTCTTACATGA GTAGCGACAATGAGTCAGATATCGAAGATGAAGACTTAAAGTTAGAGCTGCGACGACTAC GAGATAAACATCTCAAAGAGATTCAGGACCTGCAGAGTCGCCAGAAGCATGAAATTGAAT

#### FIGURE 2ZZ

CTTTGTATACCAAACTGGGCAAGGTGCCCCCTGCTGTTATTATTCCCCCAGCTGCTCCCC TTTCAGGGAGAAGACGACCCACTAAAAGCAAAGGCAGCAAATCTAGTCGAAGCAGTT CCTTGGGGAATAAAAGCCCCCAGCTTTCAGGTAACCTGTCTGGTCAGAGTGCAGCTTCAG TCTTGCACCCCAGCAGACCCTCCACCCTCCTGGCAACATCCCAGAGTCCGGGCAGAATC AGCTGTTACAGCCCTTAAGCCATCTCCCTCCAGTGACAACCTCTATTCAGCCTTCACCA GTGATGGTGCCATTTCAGTACCAAGCCTTTCTGCTCCAGGTCAAGGTAATAAAGCAACCA TCATCGTCCAAAAACAATAAAATGGAGATGTTGCCATACCTGGGACAAAAGCCTGTTAAG GCGGGTTGGGAGACTAGCTGACCAGAACACAGCCTGTGTGTTGTACACTGAAGAATCTGG GTGAAAAGGGAAGTGAGTAATGAGAATCGGTGGGCTCACTGCTCCCATTAGGTGAA ATTACTTTTTTCAAGGAATTACAGTGAAAAGTTACATCTGTGTGGCCTATATGACTTGC TCATTTGGGATTTGGAACTTAGGCTTTAATATTAGGCTGAGATTTCCTGGATGAAATTCT AAGGTGTTTTAGCAGTTTCTGAAGCTAATACATTTTCTTAGCCATTGTAGAATTTTGTTA CTTTTAAGTATGGGAGTGGCATACTAAAATGAATAACCTTACAATTCAGTTTTTTATCCA TAATCTACTTTCCAAATATAGCTCTGTTTATTAGTGATTGCTGAAAAAATTCCCACAGAG GAAAGAGCTTTTAGTCATATTAGAACAAGAATTGAAAAGACTTGGGCATCTGGGTGAGAA GAATGAAAAAATATAGGTACTGGCTTATGTGCCTTTGCCACAGTTTCACAGAAATTAGA TATTCGAACTAAGAAAAGCTTCCGCATTTTGCAGATGGGTAGAATTAAGACCTAATATTT CATCTCTTACATATCTGACCTTCCCCCCAGAAGCTTGTTCTTCTGTGTGCCATCTTAGTG TCTCTCTGTTCTACCCTGTTTTTCCCCTCTCACAGGCTGTGCGAAGTTTAACTGTGCATC TGAACAGGTGACATTCAAACCTGGTGGCAGGAGGACCCGATTTCTGAGTACGCCCTGCTT GGCTCTTTGTGTGTAACACCTTTACTCCTTCCTTGTCCTTGTGTTTCTGCTGCTTGGATC TGATGTTTCACGCAGTCCATTTTCATTTGTCTCTTTTTTGTATATCATCTACTCAGTGGCT TCAAAATAACAAGTTATCTACAAATTTCAATGTAACTTTCTGGTAGAAGTGCTTCTTCAT GGATCTGTGACAGAGAGTGGATATGGTATCTAGGCAATAGATTGCTGGGTCATTTAGAAT GAGAGAAATCAGCCAGACACGGTGGCGTACACCTGTAATCCCAGCACTTTGGGAGGCCGA GGCGGGAAGATTGCTTGAGGCCAGGAGCTCGAGACCAACCCTGGGCAACATGGTGATACC CCATCTCT

# SEQ ID NO: 64 BCON3 H

GCGGAGCGCAGCTGTGAGGGAGTCGCTGTGATCCGGGGCCCCGGAACCCGAGCTGGAGCT GGGGGAGTCCCAGACAGTACTTAGCAGTGGCTCAGACCCAAAGGTAGAATCCTCATCTTC AGCTCCTGGCCTGACATCAGTGTCACCTCCTGTGACCTCCACAACCTCAGCTGCTTCCCC AGAGGAAGAAGAAGAAGTGAAGATGAGTCTGAGATTTTGGAAGAGTCGCCCTGTGGGCG CTGGCAGAAGAGCGAGAAGAGGTGAATCAACGGAATGTACCAGGTATTGACAGTGCATA CCTGGCCATGGATACAGAGGAAGGTGTAGAGGTTGTGTGGAATGAGGTACAGTTCTCTGA ACGCAAGAACTACAAGCTGCAGGAGGAAAAGGTTCGTGCTGTGTTTGATAATCTGATTCA ATTGGAGCATCTTAACATTGTTAAGTTTCACAAATATTGGGCTGACATTAAAGAGAACAA GGCCAGGGTCATTTTTATCACAGAATACATGTCATCTGGGAGTCTGAAGCAATTTCTGAA GAAGACCAAAAAGAACCACAAGACGATGAATGAAAAGGCATGGAAGCGTTGGTGCACACA AATCCTCTCTGCCCTAAGCTACCTGCACTCCTGTGACCCCCCCATCATCCATGGGAACCT GACCTGTGACACCATCTTCATCCAGCACAACGGACTCATCAAGATTGGCTCTGTGGCTCC TGACACTATCAACAATCATGTGAAGACTTGTCGAGAAGAGCAGAAGAATCTACACTTCTT TGCACCAGAGTATGGAGAAGTCACTAATGTGACAACAGCAGTGGACATCTACTCCTTTGG CATGTGTGCACTGGAGATGCCAGTGCTGGAGATTCAGGGCAATGGAGAGTCCTCATATGT GCCACAGGAAGCCATCAGCAGTGCCATCCAGCTTCTAGAAGACCCATTACAGAGGGAGTT

400

### FIGURE 2AAA

CATTCAAAAGTGCCTGCAGTCTGAGCCTGCTCGCAGACCAACAGCCAGAGAACTTCTGTT CCACCCAGCATTGTTTGAAGTGCCCTCGCTCAAACTCCTTGCGGCCCACTGCATTGTGGG ACACCAACACATGATCCCAGAGAACGCTCTAGAGGAGATCACCAAAAACATGGATACTAG TGCCGTACTGGCTGAAATCCCTGCAGGACCAGGAAGAGAACCAGTTCAGACTTTGTACTC TCAGTCACCAGCTCTGGAATTAGATAAATTCCTTGAAGATGTCAGGAATGGGATCTATCC TCTGACAGCCTTTGGGCTGCCTCGGCCCCAGCAGCAGCAGGAGGAGGTGACATCACC TGTCGTGCCCCCTCTGTCAAGACTCCGACACCTGAACCAGCTGAGGTGGAGACTCGCAA ACTTCTGCTGAAGTTGGAGGACAAACTGAACCGGCACCTGAGCTGTGACCTGATGCCAAA TGAGAATATCCCCGAGTTGGCGGCTGAGCTGGTGCAGCTGGGCTTCATTAGTGAGGCTGA CCAGAGCCGGTTGACTTCTCTGCTAGAAGAGACCTTGAACAAGTTCAATTTTGCCAGGAA CAGTACCCTCAACTCAGCCGCTGTCACCGTCTCCTCTTAGAGCTCACTCGGGCCAGGCCC TGATCTGCGCTGTGCCTGTCCCTGGACGTGCTGCAGCCCTCCTGTCCCTTCCCCCCAGTC AGTATTACCCTGTGAAGCCCCTTCCCTCTTTATTATTCAGGAGGGCTGGGGGGGCTCCC TGGTTCTGAGCATCATCCTTTCCCCTCCCCTCTCTCCCCCTCTGCACTTTGTTTACT TGTTTTGCACAGACGTGGGCCTGGGCCTTCTCAGCAGCCGCCTTCTAGTTGGGGGCTAGT CGCTGATCTGCCGGCTCCCGCCCAGCCTGTGTGGAAAGGAGGCCCACGGGCACTAGGGGA GCCGAATTCTACAATCCCGCTGGGGCGGCCGGGGCGGAGAAAGGTGGTGCTGCAGTG GTGGCCTGGGGGGCCATTCGATTCGCCTCAGTTGCTGCTGTAATAAAAGTCTACTTTTT GCT

SEQ ID NO: 65 AA711829 M

AAACGCTGGTGTACACAGATCCTCTCTGCCCTAAGCTACCTGCACTCCTGTGACCCTCCC ATCATCCATGGGAACCTGACCTGTGACACCATCTTCATCCAGCACAACGGACTCATCAAG ATTGGCTCTGTGGCTCCTGACACTATCAACAATCACGTGAAGACTTGCCGGGAAGAACAG AAGAACCTACACTTTTTTGCACCAGAGTATGGAGAAGTCACAAACGTGACAACAGCAGTG GACATCTACTCCTTTGGCATGTGTGCACTGGAGATGGCAGTGCTGGAGATTCAGGGCAAT GGCGAGTCCTCATATGTGCCACAGGAAGCCATCAGCAGTGCCATCCAGCTACTAGAAGAC TCATTACAGAGGGAGTTTATTCAAAAGTGCCTGCAGTCTGAGCCTGCTCGGAGACCAACA GCTCACTGTATCGTGGGGCACCAACACATGATCCCAGAGAACGCTCTAGAGGAGATCACC AAGAACATGGATACCAGTGCTGTACTAGCTGAAATTCCCGCAGGGCCAGGACGAGAACCA GTTCAGACTTTGTACTCTCAGTCACCAGCCCTAGAATTAGACAAATTCCTTGAAGATGTC AGGAATGGGATCTACCCTCTGACAGCCTTTGGGCTACCTCGGCCTCAGCAGCACAGCAG GAGGAGGTGACATCACCTGTTGTGCCCCCCTCTGTCAAGACTCCAACTCCTGAGCCAGCT GAAGTGGAGACACGAAAGGTGGTGCTGATGCAGTGCAACATCGAATCTGTGGAGGAGGGA GTCAAACACCATCTAACACTTCTGCTGAAGCTGGAGGACAAATTGAACCGGCACCTGAGC TGTGACCTGATGCCAAATGAGAGCATCCCGGACTTGGCAGCTGAGCTGGTGCAGCTGGGC TTCATTAGTGAGGCTGATCAGAGCCGCCTGACTTCTCTGCTGGAGGAGACGCTCAACAAG TTCAACTTCACCAGGAACAGTACACTCAACACAGCCACTGTCACCGTCTCCTCGTAGAGC TCACTTGAGCCAGGCCCTAGCCAGGCTGTGGCTGTCCCTGGGCATGCTGCAGTCCTCCT GTCCCTTCTCCCCAGTCAGTATTACCCTTCGCGCCCATATTATTTAGGAGGGCTTTAGGG TACTTGTTTTGCACAGACGTGGGCCTGGGCCTTCTCAGCAGCCACCTTCTAGCTGGGGGC TAGTAGCTGACCTGCCTCCTGCCCTACTTGTGTGGACAGGAGGCCCACGGGCACTGG GGAAGCTGAGTTCTACAATCCCGCTGGGGCGCATGGGCAGGAGAGAAAGGTGGTGCTGCA GGGGTGGCCCCCGGGGGGGCATTCGAATCACCTCAGTTGCTGCTGTAATAAAGTCTAC TTTTTGCT

# FIGURE 2BBB

SEQ ID NO: 66\_AA099102\_H

ATGTCATCATGTGTCTCTAGCCAGCCCAGCAGCAACCGGGCCGCCCCCAGGATGAGCTG GGGGGCAGGGCAGCAGCAGCGAAAGCCAGAAGCCCTGTGAGGCCCTGCGGGGCCTC TCATCCTTGAGCATCCACCTGGGCATGGAGTCCTTCATTGTGGTCACCGAGTGTGAGCCG GGCTGTGCTGTGGACCTCGGCTTGGCGCGGGACCGGCCCCTGGAGGCCGATGGCCAAGAG GTCCCCCTTGACACCTCCGGGTCCCAGGCCCGGCCCCACCTCTCCGGTCGCAAGCTGTCT CTGCAAGAGCGGTCCCAGGGTGGGCTGGCAGCCGGTGGCAGCCTGGACATGAACGGACGC TGCATCTGCCCGTCCCTGCCCTACTCACCCGTCAGCTCCCCGCAGTCCTCGCCTCGGCTG CCCCGGCGGCCGACAGTGGAGTCTCACCACGTCTCCATCACGGGTATGCAGGACTGTGTG CAGCTGAATCAGTATACCCTGAAGGATGAAATTGGAAAGGGCTCCTATGGTGTCGTCAAG TTGGCCTACAATGAAAATGACAATACCTACTATGCAATGAAGGTGCTGTCCAAAAAGAAG CTGATCCGGCAGGCCGCTTTTCCACGTCGCCCTCCACCCCGAGGCACCCGGCCAGCTCCT GGAGGCTGCATCCAGCCCAGGGGCCCCATTGAGCAGGTGTACCAGGAAATTGCCATCCTC AAGAAGCTGGACCACCCCAATGTGGTGAAGCTGGTGGAGGTCCTGGATGACCCCAATGAG GACCATCTGTACATGGTGTTCGAACTGGTCAACCAAGGGCCCGTGATGGAAGTGCCCACC CTCAAACCACTCTCTGAAGACCAGGCCCGTTTCTACTTCCAGGATCTGATCAAAGGCATC GAGTACTTACACTACCAGAAGATCATCCACCGTGACATCAAACCTTCCAACCTCCTGGTC GGAGAAGATGGGCACATCAAGATCGCTGACTTTGGTGTGAGCAATGAATTCAAGGGCAGT GACGCGCTCCTCCAACTACGTGGGCACGCCCGCCTTCATGGCTCCCGAGTCGCTCTCT GAGACCCGCAAGATCTTCTCTGGGAAGGCCAAGGATGTTTGGGCCATGGGTGTGACACTA TACTGCTTTGTCTTTGGCCAGTGCCCATTCATGGACGAGCGGATCATGTGTTTACACAGT AAGATCAAGAGTCAGGCCCTGGAATTTCCAGACCAGCCCGACATAGCTGAGGACTTGAAG GACCTGATCACCCGTATGCTGGACAAGAACCCCGAGTCGAGGATCGTGGTGCCGGAAATC TGCACGCTGGTCGAAGTGACTGAAGAGGGGGTCGAGAACTCAGTCAAACACATTCCCAGC TTGGCAACCGTGATCCTGGTGAAGACCATGATACGTAAACGCTCCTTTGGGAACCCATTC GAGGGCAGCCGGCGGAGGAACGCTCACTGTCAGCGCCCTGGAAACTTGCTCACCAAAAA CCAACCAGGGAATGTGAGTCCCTGTCTGAGCTCAAGGAAGCAAGGCAAGCCAACCT CCAGGGCACCGACCCCCCGTGGGGGGGGGGGGGGGTGCTCTTGTGAGAGGCAGTCCC CCGGAGGAGCCCATGGAGCCCGAGTAG

SEQ ID NO: 67\_5R69\_17\_2\_H

CCGGGATGTGAGCCTGGTGGTTGGCAGCTGGAGCCACGTCGGAGGGGGAAGTGTCGCAGC ATTCTCTGCAGGCATCACAGACCTGAGGCAGTGGCCTCCGGAGGGCACTGGACAGAACA GCCATCCAAGTGGCTGAGTGGAGGGACCCTGCTCAAGTGCAGCTGCAGTGGCCGGGGTTT CAGCAGAGTGCAGGGCACCAGGAAAGGGGGCCCAGGGGAACTCCCGCGGGCCTC GCGTTTGCAAACTTCTCGCCTGGGCAGGAGGCGGTCGTGGGAAAGAAGGTGGAAGAGCGA GCTTTTTGGAACTGTGCACGGGACAGATTGGACGCACACCCCTCGGGAGGCGCGAAGGCA TGGAAAATTTGAAGCATATTATCACCCTTGGCCAGGTCATCCACAAACGGTGTGAAGAGA TGAAATACTGCAAGAAACAGTGCCGGCGCCTGGGCCACCGCGTCCTCGGCCTGATCAAGC CTCTGGAGATGCTCCAGGACCAAGGAAAGAGGAGCGTGCCCTCTGAGAAGTTAACCACAG CCATGAACCGCTTCAAGGCTGCCCTGGAGGAGGCTAATGGGGAGATAGAAAAGTTCAGCA ATAGATCCAATATCTGCAGGTTTCTAACAGCAAGCCAGGACAAAATACTCTTCAAGGACG TGAACAGGAAGCTGAGTGATGTCTGGAAGGAGCTCTCGCTGTTACTTCAGGTTGAGCAAC GCATGCCTGTTTCACCCATAAGCCAAGGAGCGTCCTGGGCACAGGAAGATCAGCAGGATG CAGACGAAGACAGCCGAGCTTTCCAGATGCTAAGAAGAGATAATGAAAAAATAGAAGCTT CACTGAGACGATTAGAAATCAACATGAAAGAAATCAAGGAAACTTTGAGGCAGTGTAAGT TATCATGTGCCCTGCTGTTTCTGATGGCCCCCAAACTAGAAGTCATCAGTTTACTGGGAC

# FIGURE 2CCC

CCCAGCCTCCCGCTACCCCTGCATTTGTCCATTTTCTGTGCTGGATGGCTGGAAGCAGCC CACAGGTTTGGGGATCCATTCATGGCTAGCCCAGGCTTCTGTCCATGGAATAACATGTGG AGAGAGCTTCTTGACCAGTAAGATACCTTCTAGCAGCTGTCAAAGTACTTAAAAACCTCT ATGAATAGAATCAAAGCTTCAGTTCAGTTGCTGAATTTCCAAGAAGAAATTCAAAT TTTAAAATGCCCACTCATTCATTCATCAACAAAACTGTGAGTATCTGGTTTATGCCAGA GGCCATGCAAAGAGGTAACTAAGATGCAGAGAAGGACACTGCCTTCCAGGAGCTCACGGG GTGGAGGAGGAAAGAGAAGACAGACAGTGAACACACAGCAAGGTTACTGAGCTTG AACTATGTCCCTAACTAGATCTGAAATGACTACGCCAGATGCCAGATGCTCAAGTGC GGTTAAGGCTGGAGGGACAGGCGGGATTTGAAGAGGGGGGAAAGGAAGTGGATGACACAT TCTGTTAACTGTCCAGCTGTGTCTCTACTGGTCACTCAGAGGCACGGGAGCCGCTCCCTT GGGCTGAGTCCATCAGAAGCCCCAGCCACCAGCTCTGGTTCATGTAGTAGAGCTTCC CACTCACACATCACAAATATGCCACCTCCCTTAGGACCCCTTCCTCTGCTCATTGACTCT CCCGCAAGAGCAAATCAAGGAGATCAAGAAGGAGCAGCTTTCAGGATCCCCGTGGATTCT GCTAAGGGAAAATGAAGTCAGCACACTTTATAAAGGAGAATACCACAGAGCTCCAGTGGC CATAAAAGTATTCAAAAAACTCCAGGCTGGCAGCATTGCAATAGTGAGGCAGACTTTCAA TAAGGAGATCAAAACCATGAAGAAATTCGAATCTCCCAACATCCTGCGTATATTTGGGAT TTGCATTGATGAAACAGTGACTCCGCCTCAATTCTCCATTGTCATGGAGTACTGTGAACT CGGGACCCTGAGGGAGCTGTTGGATAGGGAAAAAGACCTCACACTTGGCAAGCGCATGGT CCTAGTCCTGGGGGCCAGCCCGAGGCCTATACCGGCTACACCATTCAGAAGCACCTGAACT CCACGGAAAAATCAGAAGCTCAAACTTCCTGGTAACTCAAGGCTACCAAGTGAAGCTTGC AGGATTTGAGTTGAGGAAAACACAGACTTCCATGAGTTTGGGAACTACGAGAGAAAAGAC AGACAGAGTCAAATCTACAGCATATCTCTCACCTCAGGAACTGGAAGATGTATTTTATCA ATATGATGTAAAGTCTGAAATATACAGCTTTGGAATCGTCCTCTGGGAAATCGCCACTGG AGATATCCCGTTTCAAGGTGAAGAATGTGAAGACTGGCTCAGCCAGTGGCTGTAATTCTG AGAAGATCCGCAAGCTGGTGGCTGTGAAGCGGCAGCAGGAGCCACTGGGTGAAGACTGCC CTTCAGAGCTGCGGGAGATCATTGATGAGTGCCGGGCCCATGATCCCTCTGTGCGGCCCT CTGTGGATGAAATCTTAAAGAAACTCTCCACCTTTTCTAAGTAGTGTATCAAAATCTAAA ATCCTTCGGCATTGGGTTATCTATGGGTGCAAGGAGTGGGCACGCTTCTCTGTTACAAAT AGAAAACGATTCCAGTCATACAGGACACATCCCACTCCAAATGATATTTCCAAAAACATA CCTCTGACAGTAACTTTGATAGATGGTTTGTCAAATGTATCTTTCTGGGTATCCACACCT CTTGGCAATGAAATTTGCAGCTCCTCCCTTCCATAAATGAAGTCTCTTTCCCCACCATTT GAATCTGGGCTGCACTGTGACTTGATTTGATCAATAGAATGTGGAAGAAGTGACTGTAT GCCAGTTCCAAGCCTAGGTTTCAAGAGGCCTTATAAATGTCTGTTGGAACCTTACCCAGC CATGGACATGTTGAGTGAGCATGCTGGAGAATGAGAGCACATGAAGCAGAAACATGCT TCAAGACCAGAAGAACCACTCAAGCAGATCCCAGCCCAAATTGCCCATTCACACAATCAG GAGCTAAATAAATTACTGTTGTCTTTT

SEQ ID NO: 68\_H85811\_H

# FIGURE 2DDD

GCACTTCTGTCACCGGGCAAGTCCTCGGCGGACCACACACCTAATGCGTCGAAGCACTG TGAGCCTCCTTGATACCTACCAAAAATGTGGACTCAAGCGTAAGAGCGAGGAGATCGAGA ACACAAGCAGCGTGCAGATCATCGAGGAGCATCCACCCATGATTCAGAATAATGCAAGCG GGGCCACTGTCGCCACCACCACGTCTACTGCCACCTCCAAAAACAGCGGCTCCAACA GCGAGGGCGACTATCAGCTGGTGCAGCATGAGGTACTGTGCTCCATGACCAACACCTACG AGGTCTTAGAGTTCTTGGGCCGAGGGACGTTTGGGCAAGTGGTCAAGTGCTGGAAACGGG GCACCAATGAGATCGTAGCCATCAAGATCCTGAAGAACCACCCATCCTATGCCCGACAAG GTCAGATTGAAGTGAGCATCCTGGCCCGGTTGAGCACGGAGAGTGCCGATGACTATAACT TCGTCCGGGCCTACGAATGCTTCCAGCACAAGAACCACACGTGCTTGGTCTTCGAGATGT TGGAGCAGAACCTCTATGACTTTCTGAAGCAAAACAAGTTTAGCCCCTTGCCCCTCAAAT ACATTCGCCCAGTTCTCCAGCAGGTAGCCACAGCCCTGATGAAACTCAAAAGCCTAGGTC TTATCCACGCTGACCTCAAACCAGAGAACATCATGCTGGTGGATCCATCTAGACAACCAT ACAGAGTCAAGGTCATCGACTTTGGTTCAGCCAGCCACGTCTCCAAGGCTGTGTGCTCCA CCTACTTGCAGTCCAGATATTACAGGGCCCCTGAGATCATCCTTGGTTTACCATTTTGTG AGGCAATTGACATGTGGTCCCTGGGCTGTTTATTGCAGAATTGTTCCTGGGTTGGCCGT TATATCCAGGAGATTCGGAGTATGATCAGATTCGGTATATTTCACAAACACAGGGTTTGC CTGCTGAATATTTATTAAGCGCCGGGACAAAGACAACTAGGTTTTTCAACCGTGACACGG ACTCACCATATCCTTTGTGGAGACTGAAGACACCAGATGACCATGAAGCAGAGACAGGGA TTAAGTCAAAAGAAGCAAGAAAGTACATTTTCAACTGTTTAGATGATATGGCCCAGGTGA ACATGACGACAGATTTGGAAGGGAGCGACATGTTGGTAGAAAAGGCTGACCGGCGGGAGT TCATTGACCTGTTGAAGAAGATGCTGACCATTGATGCTGACAAGAGAATCACTCCAATCG AAACCCTGAACCATCCCTTTGTCACCATGACACACTTACTCGATTTTCCCCACAGCACAC CGGTGAACCAGAGCAAAACCCCTTTCATCACGCACGTGGCCCCCAGCACGTCCACCAACC TGACCATGACCTTTAACAACCAGCTGACCACTGTCCACAACCAGCCCTCAGCGGCATCCA TGGCTGCAGTGGCCCAGCGGAGCATGCCCCTGCAGACAGGAACAGCCCAGATTTGTGCCC GGCCTGACCCGTTCCAGCAAGCTCTCATCGTGTGTCCCCCCGGCTTCCAAGGCTTGCAGG CCTCTCCCTCTAAGCACGCTGGCTACTCGGTGCGAATGGAAAATGCAGTTCCCATCGTCA CTCAAGCCCCAGGAGCTCAGCCTCTTCAGATCCAACCAGGTCTGCTTGCCCAGCAGGCTT CCACCCACACCTCAGTGCAGCATGCCACCGTGATTCCCGAGACCATGGCAGCACCCAGC AGCTGGCGGACTGGAGAAATACGCATGCTCACGGAAGCCATTATAATCCCATCATGCAGC AGCCTGCACTATTGACCGGTCATGTGACCCTTCCAGCAGCACAGCCCTTAAATGTGGGTG TGGCCCACGTGATGCGGCAGCAGCCACCACCACCTCCCCGGAAGAGTAAGCAGC ACCAGTCATCTGTGAGAAATGTCTCCACCTGTGAGGTGTCCTCCTCTCAGGCCATCAGCT CCCCACAGCGATCCAAGCGTGTCAAGGAGAACACCTCCCCGCTGTGCCATGGTGCACA GTAGCCCGGCCTGCAGCACCTCGGTCACCTGTGGGTGGGCGACGTGGCCTCCAGCACCA CCCGGGAACGCCAGCGCAGACAATTGTCATTCCCGACACTCCCAGCCCCACGGTCAGCG TCATCACCATCAGCAGTGACACGGACGAGGAGGAACAGAAACACGCCCCCACCAGCA CTGTCTCCAAGCAAAGAAAAACGTCATCAGCTGTGTCACAGTCCACGACTCCCCCTACT CCGACTCCTCCAGCAACACCAGCCCCTACTCCGTGCAGCAGCGTGCTGGGCACAACAATG CCAATGCCTTTGACACCAAGGGGAGCCTGGAGAATCACTGCACGGGGAACCCCCGAACCA TCATCGTGCCACCCCTGAAAACCCAGGCCAGCGAAGTATTGGTGGAGTGTGATAGCCTGG TGCCAGTCAACACCAGTCACCACTCGTCCTCCTACAAGTCCAAGTCCTCCAGCAACGTGA CCTCCACCAGCGGTCACTCTCAGGGAGCTCATCTGGAGCCATCACCTACCGGCAGCAGC GGCCGGGCCCCACTTCCAGCAGCAGCAGCCACTCAATCTCAGCCAGGCTCAGCAGCACA TCACCACGGACCGCACTGGGAGCCACCGAAGGCAGCAGGCCTACATCACTCCCACCATGG CCCAGGCTCCGTACTCCTTCCCGCACAACAGCCCCAGCCACGGCACTGTGCACCCGCATC TGGCTGCAGCCGCTGCCCACCTCCCCACCCAGCCCCACCTCTACACCTACACTG CGCCGCCGCCCTGGGCTCCACCGGCACCGTGGCCCACCTGGTGGCCTCGCAAGGCTCTG

# FIGURE 2EEE

SEQ ID NO: 69 DYRK3 H CGGGAGCGAAAGTGCGCTGAGCTGCAGTGTCTGGTCGAGAGTACCCGTGGGAGCGTCGCG CCGCGGAGCCGTCCCGGCGTAGGTGGCGTGGCCGACCGGACCCCCAACTGGCGCCT CTCCCGAGCGGGGTCCCGAGCTAGGAGATGGGAGGCACAGCTCGTGGGCCTGGGCGGAA GGATGCGGGCCCCCGGCCCCAGCAGCGGAGTTGGGGGATGGTGTC TATGACACCTTCATGATGATAGATGAAACCAAATGTCCCCCCTGTTCAAATGTACTCTGC AATCCTTCTGAACCACCTCCACCCAGAAGACTAAATATGACCGCTGAGCAGTTTACAGGA GATCATACTCAGCACTTTTTGGATGGAGGTGAGATGAAGGTAGAACAGCTGTTTCAAGAA TTTGGCAACAGAAAATCCAATACTATTCAGTCAGATGGCATCAGTGACTCTGAAAAATGC TCTCCTACTGTTTCTCAGGGTAAAAGTTCAGATTGCTTGAATACAGTAAAATCCAACAGT TCATCCAAGGCACCCAAAGTGGTGCCTCTGACTCCAGAACAAGCCCTGAAGCAATATAAA CACCACCTCACTGCCTATGAGAAACTGGAAATTAATTATCCAGAAATTTACTTTGTA GGTCCAAATGCCAAGAAAAGACATGGAGTTATTGGTGGTCCCAATAATGGAGGGTATGAT GATGCAGATGGGGCCTATATTCATGTACCTCGAGACCATCTAGCTTATCGATATGAGGTG CTGAAAATTATTGGCAAGGGGAGTTTTGGGCAGGTGGCCAGGGTCTATGATCACAAACTT CGACAGTACGTGGCCCTAAAAATGGTGCGCAATGAGAAGCGCTTTCATCGTCAAGCAGCT GAGGAGATCCGGATTTTGGAGCATCTTAAGAAACAGGATAAAACTGGTAGTATGAACGTT ATCCACATGCTGGAAAGTTTCACATTCCGGAACCATGTTTGCATGGCCTTTGAATTGCTG AGCATAGACCTTTATGAGCTGATTAAAAAAAAATAAGTTTCAGGGTTTTAGCGTCCAGTTG GTACGCAAGTTTGCCCAGTCCATCTTGCAATCTTTGGATGCCCTCCACAAAAATAAGATT ATTCACTGCGATCTGAAGCCAGAAAACATTCTCCTGAAACACCACGGGCGCAGTTCAACC AAGGTCATTGACTTTGGGTCCAGCTGTTTCGAGTACCAGAAGCTCTACACATATATCCAG TCTCGGTTCTACAGAGCTCCAGAAATCATCTTAGGAAGCCGCTACAGCACCAATTGAC ATATGGAGTTTTCGCTGCATCCTTGCAGAACTTTTAACAGGACAGCCTCTCTTCCCTGGA GAGGATGAAGGAGACCAGTTGGCCTGCATGATGGAGCTTCTAGGGATGCCACCACCAAAA CTTCTGGAGCAATCCAAACGTGCCAAGTACTTTATTAATTCCAAGGGCATACCCCGCTAC TGCTCTGTGACTACCCAGGCAGATGGGAGGGTTGTGCTTGTGGGGGGGTCGCTCACGTAGG GGTAAAAAGCGGGGTCCCCCAGGCAGCAAAGACTGGGGGGACAGCACTGAAAGGGTGTGAT GACTACTTGTTTATAGAGTTCTTGAAAAGGTGTCTTCACTGGGACCCCTCTGCCCGCTTG ACCCCAGCTCAAGCATTAAGACACCCTTGGATTAGCAAGTCTGTCCCCAGACCTCTCACC ACCATAGACAAGGTGTCAGGGAAACGGGTAGTTAATCCTGCAAGTGCTTTCCAGGGATTG GGTTCTAAGCTGCCTCCAGTTGTTGGAATAGCCAATAAGCTTAAAGCTAACTTAATGTCA GAAACCAATGGTAGTATACCCCTATGCAGTGTATTGCCAAAACTGATTAGCTAGTGGACA GAGATATGCCCAGAGATGCATATGTGTATATTTTTATGATCTTACAAACCTGCAAATGGA AAAAATGCAAGCCCATTGGTGGATGTTTTTGTTAGAGTAGACTTTTTTTAAACAAGACAA AACATTTTTATATGATTATAAAAGAATTCTTCAAGGGCTAATTACCTAACCAGCTTGTAT TGGCCATCTGGAATATGCATTAAATGACTTTTTATAGGTCA

### **FIGURE 2FFF**

SEQ ID NO: 70\_AA589241\_M DYRK3\_M
CCACGCGTCCGGAGTTGCTAGGAATGCCACCGCAGAAACTTCTGGAGCAATCCAAGCGTG
CCAAGTACTTTATTAACTCCAAAGGCTTGCCTCGATACTGCTCCGTATCTACCCAGACGG
ACGGGAGGGTGGTGCTTCTCGGGGGTCGCTCACGCAGGGGTAAAAAGCGAGGCCCGCCAG
GCAGCAAAGACTGGGCAACCGCACTGAAGGGCTGTGGTGACTACTTGTTCATAGAGTTTC
TGAAACGATGCCTCCAGTGGGACCCCTCTGCCCGCCTCACCCCGGCTCAAGCATTAAGAC
ATCCTTGGATTAGCAAGTCTACACCCAAACCTCTCACCATGGACAAGGTGCCAGGGAAGC
GGGTAGTTAACCCTACAAATGCTTTCCAGGGACTGGGTTCCAAGCTGCCTCCAGTCGTTG
GGATAGCCAGTAAGCTTAAAGCTAACCTAATGTCCGAAACCAGTGGTAGTATACCTCTGT
GCAGTGTATTGCCAAAGCTGATTAGCTAGTGGACCACTCAGAGACTGATACATATCATAT
GTATTTTTAATTACCTTGCAAACATGCAAATGGAAAACGGAATAATTGAAGCCATTCAC
TGATGGATATGTTTTTTTTTAGACTTTTTTTTAACAAGGCAGAACATTTTTATATGACTAT
AAAAGAACGCTTCAAGGGCTAATGTCAAACCAGCTTGTATTGGCCATCTGGAGTATACAT

SEQ ID NO: 71 5R72 16 2 H GTCGAGGCGCAGCGCTGCCATGGCTGGGGGCCCTGGGGCCCGGGGCCGGGACGA GCCTCCGGAGAGCTACCCGCAACGACAGGACCACGAGCTACAGGCCCTGGAGGCCATCTA CGGCGCGACTTCCAAGACCTGCGGCCGGACGCTTGCGGACCGGTCAAAGAGCCCCCTGA AATCAATTTAGTTTTGTACCCTCAAGGCCTAACTGGTGAAGAAGTATATGTAAAAGTGGA TTTGAGGGTTAAATGCCCACCTACCTATCCAGATGTAGTTCCTGAAATAGAGTTAAAAAA TGCCAAAGGTCTATCAAATGAAAGTGTCAATTTGTTAAAATCTCGCCTAGAAGAACTGGC CAAGAAACACTGTGGGGAGGTGATGATCTTTGAACTGGCTTACCACGTGCAGTCATTTCT CAGCGAGCATAACAAGCCCCCTCCCAAGTCTTTTCATGAAGAAATGCTGGAAAGGCGGGC TCAGGAGGAGCAGCAGAGGCTGTTGGAGGCCAAGCGGAAAGAAGAGCAGGAGCAACGTGA AATCCTGCATGAGATTCAGAGAAGGAAAGAAGAGAGAAAAAAGGAAAAAAGGAAAGA AATGGCTAAGCAGGAACGTTTGGAAATTGCTAGTTTGTCAAACCAAGATCATACCTCTAA GAAGGACCCAGGAGGACACAGAACGGCTGCCATTCTACATGGAGGCTCTCCTGACTTTGT AGGAAATGGTAAACATCGGGCAAACTCCTCAGGAAGGTCTAGGCGAGAACGTCAGTATTC TGTATGTAATAGTGAAGATTCTCCTGGCTCTTGTGAAATTCTGTATTTCAATATGGGGAG TCCTGATCAGCTCATGGTGCACAAAGGGAAATGTATTGGCAGTGATGAACAACTTGGAAA ATTAGTCTACAATGCTTTGGAAACAGCCACTGGTGGCTTTGTCTTGTTGTATGAGTGGGT CCTTCAGTGGCAGAAAAAATGGGTCCATTCCTTACCAGTCAAGAAAAAGAGAAGATTGA TAAGTGCAAAAAGCAGATTCAAGGAACAGAAACAGAATTCAACTCACTGGTAAAATTGAG CCATCCAAATGTAGTACGCTACCTTGCAATGAATCTCAAAGAGCCAAGACGACTCCATCGT GGTGGACATTTTAGTGGAGCACATTAGTGGGGTCTCTCTTGCTGCACACCTGAGCCACTC AGGCCCCATCCCTGTGCATCAGCTTCGCAGGTACACAGCTCAGCTCCTGTCAGGCCTTGA TTATCTGCACAGCAATTCTGTGGTGCATAAGGTCCTGAGTGCATCTAATGTCTTGGTGGA TGCAGAAGGCACCGTCAAGATTACGGACTATAGCATTTCTAAGCGCCTCGCAGACATTTG CAAGGAGGATGTTTTGAGCAAACCCGAGTTCGTTTTAGTGACAATGCTCTGCCTTATAA AACGGGGAAGAAGGAGATGTTTGGCGTCTTGGCCTTCTGCTGCTGTCCCTCAGCCAAGG ACAGGAATGTGGAGAGTACCCTGTGACCATCCCTAGTGACTTACCAGCTGACTTTCAAGA TTTTCTAAAGAAATGTGTGTGCTTGGATGACAAGGAAAGATGGAGTCCCCAGCAGTTGTT GAAACACAGCTTTATAAATCCCCAGCCAAAAATGCCTCTAGTGGAACAAAGTCCTGAAGA TTCTGGAGGACAAGATTATGTTGAGACTGTTATTCCTAGCAACCGGCTACCCAGTGCTGC CTTCTTTAGTGAGACACAGAGACAGTTTTCCCGATACTTCATTGAGTTTGAAGAATTACA ACTTCTTGGTAAAGGAGCTTTTGGAGCTGTCATCAAGGTGCAGAACAAGTTGGACGGCTG CTGCTACGCAGTGAAGCGCATCCCCATCAACCCGGCCAGCCGGCAGTTCCGCAGGATCAA GGGCGAAGTGACACTGCTGTCACGGCTGCACCATGAGAACATTGTGCGCTACTACAACGC CTGGATCGAGCGGCACGAGCGGCCGGGGGACCGGGCCCCCGGACTCCGGGCC

PCT/US00/14842

### FIGURE 2GGG

CAGCGTAGAGGCCGCCGCCCCCCCCCCTCCTCAGCAGCTCGGTGGAGTGGAGCACTTC GGGCGAGCGCTCGGCCAGTGCCCGTTTCCCCGCCACCGGCCCCGGGCTCCAGCGATGACGA TTCTGAAAGTGATATTATCTTTGACAATGAAGATGAGAACAGTAAAAGTCAGAATCAGGA TGAAGATTGCAATGAAAAGAATGGCTGCCATGAAAGTGAGCCATCAGTGACGACTGAGGC TGTGCACTACCTATACATCCAGATGGAGTACTGTGAGAAGAGCACTTTACGAGACACCAT TGACCAGGGACTGTATCGAGACACCGTCAGACTCTGGAGGCTTTTTCGAGAGATTCTGGA TGGATTAGCTTATATCCATGAGAAAGGAATGATTCACCGGGATTTGAAGCCTGTCAACAT TTTTTTGGATTCTGATGACCATGTGAAAATAGGTGATTTTGGTTTTGGCGACAGACCATCT AGCCTTTCTGCTGACAGCAAACAAGACGATCAGACAGGAGACTTGATTAAGTCAGACCC TTCAGGTCACTTAACTGGGATGGTTGGCACTGCTCTCTATGTAAGCCCAGAGGTCCAAGG AAGCACCAAATCTGCATACAACCAGAAAGTGGATCTCTTCAGCCTGGGAATTATCTTCTT CAGAGATCCCACTTCGCCTAAGTTTCCAGAAGACTTTGACGATGGAGAGCATGCAAAGCA GAAATCAGTCATCTCCTGGCTGTTGAACCACGATCCAGCAAAACGGCCCACAGCCACAGA GCTGCTCAAGAGTGAGCTGCTGCCCCCACCCCAGATGGAGGAGTCAGAGCTGCATGAAGT GCTGCACCACACGCTGACCAACGTGGATGGGAAGGCCTACCGCACCATGATGGCCCAGAT CTTCTCGCAGCGCATCTCCCCTGCCATCGATTACACCTATGACAGCGACATACTGAAGGG CTTTAAAAGACATGGAGCTGTTCAGTTGTGTACTCCACTACTGCTTCCCCGAAACAGACA AATATATGAGCACAACGAAGCTGCCCTATTCATGGACCACAGCGGGATGCTGGTGATGCT TCCTTTTGACCTGCGGATCCCTTTTGCAAGATATGTGGCAAGAAATAATATATTGAATTT AAAACGATACTGCATAGAACGTGTGTTCAGGCCGCGCAAGTTAGATCGATTTCATCCCAA AGAACTTCTGGAGTGTGCATTTGATATTGTCACTTCTACCACCAACAGCTTTCTGCCCAC TGCTGAAATTATCTACACTATCTATGAAATCATCCAAGAGTTTCCAGCACTTCAGGAAAG **AAATTACAGTATTTATTTGAACCATACCATGTTATTGAAAGCAATACTCTTACACTGTGG** GATCCCAGAAGATAAACTCAGTCAAGTCTACATTATTCTGTATGATGCTGTGACAGAGAA GCTGACGAGGAGAAGTGGAAGCTAAATTTTGTAATCTGTCTTTGTCTTCTAATAGTCT GTGTCGACTCTACAAGTTTATTGAACAGAAGGGAGATTTGCAAGATCTTATGCCAACAAT AAATTCATTAATAAAACAGAAAACAGGTATTGCACAGTTGGTGAAGTATGGCTTAAAAGA CCTAGAGGAGGTTGTTGGACTGTTGAAGAAACTCGGCATCAAGTTACAGGTCTTGATCAA TTTGGGCTTGGTTTACAAGGTGCAGCACAATGGAATCATCTTCCAGTTTGTGGCTTT CATCAAACGAAGGCAAAGGGCTGTACCTGAAATCCTCGCAGCTGGAGGCAGATATGACCT GCTGATTCCCCAGTTTAGAGGGCCACAAGCTCTGGGGCCAGTTCCCACTGCCATTGGGGT CAGCATAGCTATAGACAAGATATCTGCTGCTGTCCTCAACATGGAGGAATCTGTTACAAT AAGCTCTTGTGACCTCCTGGTTGTAAGTGTTGGTCAGATGTCTATGTCCAGGGCCATCAA CCTAACCCAGAAACTCTGGACAGCAGGCATCACAGCAGAAATCATGTACGACTGGTCACA GTCCCAAGAGGAATTACAAGAGTACTGCAGACATCATGAAATCACCTATGTGGCCCTTGT GAAGCGTGTGCTGGAGACTGAACTTGTGGACCATGTACTGCAGAAACTGAGGACTAAAGT CACTGATGAAAGGAATGGCAGAGAAGCTTCCGATAATCTTGCAGTGCAAAATCTGAAGGG GTCATTTCTAATGCTTCAGGTTTGTTTGAAATCCATGGAGCAACAGTGGTTCCCATTGT GAGTGTGCTAGCCCCGGAGAAGCTGTCAGCCAGCACTAGGAGGCGCTATGAAACTCAGGT ACAAACTCGACTTCAGACCTCCCTTGCCAACTTACATCAGAAAAGCAGTGAAATTGAAAT TCTGGCTGTGGATCTACCCAAAGAAACAATATTACAGTTTTTATCATTAGAGTGGGATGC TGATGAACAGGCATTTAACACAACTGTGAAGCAGCTGCTGTCACGCCTGCCAAAGCAAAG ATACCTCAAATTAGTCTGTGATGAAATTTATAACATCAAAGTAGAAAAAAAGGTGTCTGT GCTATTTCTGTACAGCTATAGAGATGACTACTACAGAATCTTATTTTAACCCTAAAGAAC TGTCGTTAACCTCATTCAAACAGACAGAGGCTTATACTGGAATAATGGAATGTTGTACAT

### FIGURE 2HHH

TCATCATAATTAAAATTAAATTCTAAGAAGAGGCTGGGTGCAGTGGCTCACACCTTTAA TCCCAGCACTTTGGGAAGCCAAGGCAGGAAGACTGCTTGAAACCAGGAGTTTGAGACCAG CCT

SEQ ID NO: 73\_R43524\_H, HRI\_H GTGGCTGCCCCGCCGACCTTTCCCGCCGAGGCCCCGACCCCGAATATGACGAA TCTGATGTTCCAGCAGAAATCCAGGTGTTAAAAGAACCCCTACAACAGCCAACCTTCCCT TTTGCAGTTGCAAACCAACTCTTGCTGGTTTCTTTGCTGGAGCACTTGAGCCACGTGCAT GAACCAAACCCACTTCGTTCAAGACAGGTGTTTAAGCTACTTTGCCAGACGTTTATCAAA ATGGGGCTGTTGTCTTTCACTTGTAGTGACGAGTTTAGCTCATTGAGACTACATCAC GAGGATATTTCTCGTATCCAGAAAATCAGATCAAGGGAAGTAGCCTTGGAAGCACAAACT TCACGTTACTTAAATGAATTTGAAGAACTTGTCATCTTAGGAAAAGGTGGATACGGAAGA GTATACAAGGTCAGGAATAAATTAGATGGTCAGTATTATGCAATAAAAAAATCCTGATT AAGGGTGCAACTAAAACAGTTTGCATGAAGGTCCTACGGGAAGTGAAGGTGCTGGCAGGT CTTCAGCACCCCAATATTGTTGGCTATCACACCGCGTGGATAGAACATGTTCATGTGATT CAGCCACGAGCAGACAGAGCTGCCATTGAGTTGCCATCTCTGGAAGTGCTCTCCGACCAG GAAGAGGACAGAGCAATGTGGTGTTAAAAATGATGAAAGTAGCAGCTCATCCATTATC TTTGCTGAGCCCACCCCAGAAAAAGAAAACGCTTTGGAGAATCTGACACTGAAAATCAG AATAACAAGTCGGTGAAGTACACCACCAATTTAGTCATAAGAGAATCTGGTGAACTTGAG TCGACCCTGGAGCTCCAGGAAAATGGCTTGGCTGGTTTGTCTGCCAGTTCAATTGTGGAA CAGCAGCTGCCACTCAGGCGTAATTCCCACCTAGAGGAGAGTTTCACATCCACCGAAGAA TCTTCCGAAGAAAATGTCAACTTTTTGGGTCAGACAGAGGCACAGTACCACCTGATGCTG CACATCCAGATGCAGCTGTGAGCTCTCGCTGTGGGATTGGATAGTCGAGAGAACAAG CGGGGCCGGGAGTATGTGGACGAGTCTGCCTGTCCTTATGTTATGGCCAATGTTGCAACA CGAGATCTGAAGCCAAGAAATATTTTTCTTCATGGCCCTGATCAGCAAGTAAAAATAGGA GACTTTGGTCTGGCCTGCACAGACATCCTACAGAAGAACACAGACTGGACCAACAGAAAC GGGAAGAGACACCAACACATACGTCCAGAGTGGGTACTTGTCTGTACGCTTCACCCGAA CAGTTGGAAGGATCTGAGTATGATGCCAAGTCAGATATGTACAGCTTGGGTGTGGTCCTG AGAACTGGTCAGTTGCCGGAATCCCTCCGTAAAAGGTGTCCAGTGCAAGCCAAGTATATC CAGCACTTAACGAGAAGGAACTCATCGCAGAGACCATCTGCCATTCAGCTGCTGCAGAGT GAACTTTTCCAAAATTCTGGAAATGTTAACCTCACCCTACAGATGAAGATAATAGAGCAA GAAAAAGAAATTGCAGAACTAAAGAAGCAGCTAAACCTCCTTTCTCAAGACAAAGGGGTG AGGGATGACGGAAAGGATGGGGGCGTGGGATGA

### FIGURE 2111

AGGTTTTGGCTCGAATGCACGATGAAGACCTCATTCATGGTGATCTCACCACCTCCAACA TGCTCCTGAAACCCCCCCTGGAACAGCTGAACATTGTGCTCATAGACTTTGGGCTGAGTT TCATTTCAGCACTTCCAGAGGATAAGGGAGTAGACCTCTATGTCCTGGAGAAGGCCTTCC TCAGTACCCATCCCAACACTGAAACTGTGTTTGAAGCCTTTCTGAAGAGCTACTCCACCT CCTCCAAAAAGGCCAGGCCAGTGCTAAAAAAATTAGATGAAGTGCGCCTGAGAGGAAGAA TCAAAGTAAATTTGAAGAAATGCTACAAGTATGAGATGAGATCTAAGTAAAGGTGTTAAG ATATTTTTAAGTGGTATGTGATCGTGTCATTATCATCTGCACTTCACTCAAGAGCTTACT ATGTGTCTAAGTCATGTTCTAGGCAGAATTGGGTATTTAAAGTAAATTGAGGACAGGCTT CTCCCAGATTGTGACATGTATATCTCAGATACATGGGTGTGGCATTGAACCACATAATGA GAACATTATTCTCTTTTTAGTCCTTGTGAGACAAGGATGAAGTCTCAGTTGCTGATACTC ATTTATTTTGAAACCAGTTTAATGGGATACAACCAGCATTTTAAAAAAATGAAATAGAATA GATATGTGCTGAGTTTTGATGTCAAATATATTTCTCTTTCAGGGTCATGATCAAAAAATG AAAAGTCTGCTTAACTCCAATTTCTCTTTTAAAAAAGCAGACTTACAGCTTTCAGGCAAC TGAAATTCATGTTAACATGTTTTTATTTTTTTTTGTGTATTTTTTGTGGTTACCTTCTA TTCTATCACAGGCAGTAAGTAGGTAGAGCAAAAATGGTGAAGTGACTTGTGAAGACTGAA GTTTGATGAAGTCTGGTTTAAGGCACAGGTAAACTGAGTGTGGATGCAAAAGTACCAGGA TATTTTGAGTGCCTTTTGTGTTCCTTGGCACCCTGTTGGGTATTGGGTACTTGGCACCCT GTTGGGTATTGGGTACAATGGTGAGCCAGACAGACACAGCGCCTGTCCTTTTGTAAGAAT ATTTATTTTTATAAAAAAGTATAAAGTATACAGTGGGATGTTTTGATATACATTATGAAA TGATTGCTACAGCTGAGCTAATTAACACCCATCACCTCACATAGTTACTGTCTTGTTTCT TAATATGGACATTTGCAGCTATGAATTTCCCTCTGCACACTGTTGTCATCACACACTCTC AGTTTTGGTATTTTGTGTTTTTGTTTTCATTCATCTCAAAGTATTTTCTAATTTCCCTTG TGATTTCTTCTTTGACCCCTTGATTGTTTAGAAATCTGTTAATTTCCACACATTTGTAAA TGTTCCAATTTTTCTTTTGTTATTGCCAGCTTCATTCCATTGTGTTCAGAGATGATACAG TCATTCACCACAGTCAGCATGCCCCAAGTGCCCAGCATGGGGCGGATGGCCAGGAATGAG TGAAAACTTCCCTTCCTGGGTAGTTGTGACTAGTAGAGAGGAAAAATAATATAATTGCCT GCTTACTGCATGCCAGGCATTGGGCTGGGAATTTTTATATTGGATCTAAAATAACTCTTA AGTTAGGCATTATCCCCATTTTATAGATGGAGAAACTGGCCCCAAAAGGTGGGAACTTGT CCAAGACGTCACAGGTAGCAAGAGGTACTTTTACCTGGCTCCAAATCTGTGTTCTTTCCA CTGACAAATGAGATATGGGATATGGTGCATCTTTACAGTACTATAATAAGTATTGGCGTA TAACATTATTTTCAAGGAACTCCAAGGGCCACAGGAGCTGACAGGTTTTTCAATTAATAT TCCCAACATGAATGAGATGCCTCATTCCTCAGTTTCCTCACGTGTACTATAAGGCTAGTA CCTGCTTTGTTGGGGTATGGTTGGCTCGTGTGCATTAAGTCAACAAATCCCTAGT

 WO 00/73469 PCT/US00/14842

#### FIGURE 2JJJ

SEQ ID NO: 76 17000139801197 H, IRAKM H ATGGCGGGGAACTGTGGGGCCCGCGCGCGCTGTCGGCGCACACGCTGCTGTTCGACCTG TATGTAGACCAAGGTAAAAGTGGAACAAGAGAATTACTTTGGTCCTGGGCACAGAAAAAC AAGACCATCGGTGACCTTTTACAGGTCCTCCAGGAGATGGGACATCGTCGAGCTATTCAT TTAATTACAAACTATGGAGCAGTGTTGAGTCCTTCAGAGAAGAGTTATCAGGAAGGTGGA TTTCCAAATATATTATTCAAGGAAACAGCCAATGTCACCGTGGATAATGTTCTTATTCCT GAACATAATGAAAAAGGAGTACTGCTTAAATCTTCCATCAGCTTTCAAAATATCATAGAA GGAACTAGAAATTTCCACAAAGACTTCCTAATTGGAGAAGGAGAGATTTTTGAGGTATAC AGAGTGGAGATTCAAAACCTAACATATGCTGTCAAATTATTTAAACAGGAGAAAAAAATG CAGTGTAAGAAGCATTGGAAGAGGTTTTTATCTGAGCTTGAAGTTTTACTACTGTTTCAT TATCCATACATGAGAAATGGAACACTTTTTGACAGATTGCAGTGTGTAGGTGACACGGCC CCACTCCCTTGGCACATTCGAATCGGTATATTAATAGGAATATCCAAAGCCATTCACTAC CTGCACAACGTTCAACCATGCTCGGTCATCTGTGGCAGTATATCAAGTGCAAACATCCTT TTGGATGATCAGTTTCAACCCAAACTAACTGATTTTGCCATGGCACACTTCCGGTCCCAC CTAGAACATCAGAGTTGTACCATAAATATGACCAGCAGCAGCAGTAAACATCTGTGGTAC ATGCCAGAAGAGTACATCAGACAGGGGAAACTTTCCATTAAAACAGATGTCTACAGCTTT GGAATTGTAATAATGGAAGTTCTAACAGGATGTAGAGTAGTGTTAGATGATCCAAAACAT ATCCAGCTGCGGGATCTCCTTAGAGAATTGATGGAGAAGAGAGGCCTGGATTCATGTCTC TCATTTCTAGATAAGAAAGTGCCTCCCTGCCCTCGGAATTTCTCTGCCAAGCTCTTCTGT TTGGCAGGCCGGTGTGCTGCAACGCGGGCAAAGTTAAGACCATCAATGGATGAAGTTTTA AATACTCTTGAAAGTACTCAAGCCAGCTTGTATTTTGCTGAAGATCCTCCCACATCACTA AAGTCCTTCAGGTGTCCTTCTCTCTATTCCTGGAGAATGTACCAAGTATTCCAGTGGAA GATGATGAAAGCCAGAATAACAATTTACTACCTTCTGATGAAGGCCTGAGGATAGACAGA ATGACTCAGAAAACTCCTTTTGAATGCAGCCAGTCTGAGGTTATGTTTCTGAGCTTGGAC AAAAAGCCAGAGAGAAAATGAGGAAGCTTGCAACATGCCCAGTTCTTCTTGTGAA GAAAGTTGGTTCCCAAAGTATATAGTTCCATCCCAGGACTTAAGGCCCTATAAGGTAAAT ATAGATCCTTCTTCAGAAGCTCCAGGGCATTCTTGCAGGAGCAGGCCAGTGGAGAGCAGC TGTTCCTCCAAATTTTCCTGGGATGAATATGAACAGTACAAAAAAGAATAA

SEQ ID NO: 77\_AA840598\_M IRAKM\_M
ATGTGGAAGAGTTTTTATCAGAACTGGAAGTTCTACTCCTGTTCCGTCACCCCACATA
CTAGAGCTGGCTGCATATTTCACGGAGACTGAGAAACTTTGTCTGGTTTATCCCTATATG
AGCAACGGGACGCTTTTCGACAGATTACAGTGCACAAATGGCACAACCCCGCTTTCCTGG
CACGTTCGAATCAGCGTATTGATAGGAATAGCCAAAGCCATCCAATACTTGCACAACACT
CAGCCGTGCGCCGTCATCTGTGGCAACGTTTCCAGTGCAAACATACTCTTGGATGACCAG
CTCCAACCCAAACTAACGGATTTTGCTGCAGCGCACTTCCGACCCAATCTAGAGCAGCAG
AGTTCTACCATAAATATGACCGGCGGTGGCAGGAAACATCTGTGGTACATGCCAGAAGAA

PCT/US00/14842

#### FIGURE 2KKK

TACATCAGACAGGGAAGACTTTCCGTTAAAACTGATGTCTACAGCTTCGGAATCGTGATC ATGGAGGTTCTAACGGGCTGCAAAGTGGTGCTGGATGACCCGAAACACGTTCAGCTGCGG AGGAAGATACCACCCTGTCCTCGGAACTTCTCTGCAAAGCTCTTCTCTCTGGCGGGCCGG TGTGTGGCAACGAAGGCCAAGTTAAGACCCACGATGGACGAAGTCCTGTCCTCTCTGGAG AGCACCCAGCCTAGCTTGTATTTTGCAGAAGACCCTCCCACGTCCTTGAAGTCCTTCAGG TGTCCTTCTCCACTGTTCTTGGATAATGTCCCAAGTATTCCAGTAGAAGATGATGAAAAC CAGAATAACCATTCAGTACCTCCCAAGGAAGTTTTGGGGACAGATAGAGTGACTCAGAAA ACCCCTTTGAATGCAGCCAGTCTGAGGTCACCTTTCTAGGCTTGGACCGAAACAGAGGG AACAGGGGAAGTGAAGCGGATTGCAACGTGCCCAGTTCTTCTCATGAGGAATGCTGGTCC CCAGAGCTTGTGGCGCCATCCCAGGACTTAAGTCCTACTGTGATCAGTTTGGGCTCGTCT TGGGAAGTACCAGGCCATTCTTATGGGAGCCAAGCCAATGGAGAAGAGGTGTTCCTCTGGG CTCTTTTGCAGTGAGCATGAACAGTCCAAAAAGCAGTGAATCCACCAGAAGATCAAGCAA AAAATAAAGCAAACGTCACTGAAGGCACTGAGCAAATAGCATCCCCGTGAAAAGACACG AGCTCTGAGCTCCGTGAGTACAGCCAAGGGACCAACTGATGGAGAATTTGAATGGTGCAG ATTAGCAGCAAGGAAGTCTATTCCTTCCTCCAAACAGAATAATTTCAAGAGATGCTTTAT TCAAGTGACCGCCTCTCAGTCAAACCTGAGAAGCTAAACTGGAGCCAATCAGAATTATCC AAGATTCCGGGTTCTGACAACCAAAACCTAGCAAAGAGTAGCAGGACAAGTCTCTCTT **AAGTCTCTCACTCTCTCATCATCCGAGTGAGATCTTGGTATAGGTGAACAGAGAACCA** GCAGCCAGTAGTCACCAGCCAGTCATCATGATACAGTGTCACTCTCCCTCTGCGCATGCC TCTGTTGCGTAGTGTGACTTTGTGGCATGACTTGGTTGTCAGATCATTTGCACAAGAACA AGCGAATACACAACAACAAGCCCACCATCATTACCACCGGCACTTAATGCTAGTCTTTC TGCTAGGGATACTGACAGTCTATTTGCTTCCCATGGTCATAGGGAAGTTGCTCAAATGCA TTTTACAGCCAGTTGCTACTCTTGTTTATCGCTGGTTAACCGGTCTGTCCGGAAGTGAGC CAAGTCATCCTTGCTAGGGCTTTTTCTGTGTAGAGAGGGAATTCCAGTCCAAAGTCTGCT TCTCTGTATTTAAATTCTTAGAAGAGTTGCCTGTGGCATTCCAATTGTTATATAAAAAAA TTATATTAAAGAATTCCAGCACT

SEQ ID NO: 78 AA088547 H

ATGGCGAGTGCGGTCAGGGGGTCGAGGCCGTGGCCCCGGGCTGGGGCTCCAGCTCCAGTTC GCGGCGCTGCTCGGGACGCTGAGTCCACAGGTTCATACTCTCAGGCCAGAGAACCTC AAGTGGACTCTGAGGGATGATCCCGTCATCGAAGGACCAATGTACGTCACAGAAATGGCC TTTCTCTCTGACCCAGCAGATGGCAGCCTGTACATCTTGGGGACCCAAAAACAACAGGGA TTAATGAAACTGCCATTCACCATCCCTGAGCTGGTTCATGCCTCTCCCTGCCGCAGCTCT GATGGGGTCTTCTACACAGGCCGGAAGCAGGATGCCTGGTTTGTGGTGGACCCTGAGTCA GGGGAGACCCAGATGACACTGACCACAGAGGGTCCCTCCACCCCCGCCTCTACATTGGC CGAACACAGTATACGGTCACCATGCATGACCCAAGAGCCCCAGCCCTGCGCTGGAACACC ACCTACCGCCGCTACTCAGCGCCCCCATGGATGGCTCACCTGGGAAATACATGAGCCAC CTGGCGTCCTGCGGGATGGGCCTGCTGCTCACTGTGGACCCAGGAAGCGGGACGGTGCTG TGGACACAGGACCTGGGCGTGCCTGTGATGGGCGTCTACACCTGGCACCAGGACGGCCTG CGCCAGCTGCCGCATCTCACGCTGGCTCGAGACACTCTGCATTTCCTCGCCCTCCGCTGG GGCCACATCCGACTGCCTGCCTCAGGCCCCCGGGACACAGCCACCCTCTTCTCTACCTTG GACACCCAGCTGCTAATGACGCTGTATGTGGGGAAGGATGAAACTGGCTTCTATGTCTCT AAAGCACTGGTCCACACAGGAGTGGCCCTGGTGCCTCGTGGACTGACCCTGGCCCCCGCA GATGGCCCCACCACAGATGAGGTGACACTCCAAGTCTCAGGAGAGCGAGAGGGCTCACCC WO 00/73469 PCT/US00/14842

### FIGURE 2LLL

AGCACTGCTGTTAGATACCCCTCAGGCAGTGTGGCCCTCCCAAGCCAGTGGCTGCTCATT GGACACCACGAGCTACCCCCAGTCCTGCACACCACCATGCTGAGGGTCCATCCCACCCTG GGGAGTGGAACTGCAGAGACAAGACCTCCAGAGAATACCCAGGCCCCAGCCTTCTTCTTG GAGCTATTGAGCCTGAGCCGAGAGAAACTTTGGGACTCCGAGCTGCATCCAGAAGAAAA ACTCCAGACTCTTACTTGGGGCTGGGACCCCAAGACCTGCTGGCAGCTAGCCTCACTGCT GTCCTCCTGGGAGGGTGGATTCTCTTTGTGATGAGGCAGGTGGTGGAGAAGCAGCAGGAG ACCCCCTGGCACCTGCAGACTTTGCTCACATCTCCCAGGATGCCCAGTCCCTGCACTCG GACGACCCTGAAGCTGAGCAACTCACCGTAGTGGGGAAGATTTCCTTCAATCCCAAGGAC GTGCTGGGCCGGGGCAGGCGGGACTTTCGTTTTCCGGGGACAGTTTGAGGGACGGCCA GTGGCTGTCAAGCGGCTCCTCCGCGAGTGCTTTGGCCTGGTTCGGCGGGAAGTTCAACTG CTGCAGGAGTCTGACAGGCACCCCAACGTGCTCCGCTACTTCTGCACCGAGCGGGGACCC CAGTTCCACTACATTGCCCTGGAGCTCTGCCGGGCCTCCTTGCAGGAGTACGTAGAAAAC CCGGACCTGGATCGCGGGGTCTGGAGCCCGAGGTCGTGCTGCAGCAGCTGATGTCTGGC CTGGCCCACCTGCACTCTTTACACATAGTGCACCGGGACCTGAAGCCAGGAAATATTCTC ATCACCGGGCCTGACAGCCAGGGCCTGGGCAGAGTGGTGCTCTCAGACTTCGGCCTCTGC AAGAAGCTGCCTGCCGCCTGTAGCTTCAGCCTCCACTCCGGCATCCCCGGCACGGAA GGCTGGATGGCGCCCGAGCTTCTGCAGCTCCTGCCACCAGACAGTCCTACCAGCGCTGTG GACATCTTCTCTGCAGGCTGCGTGTTCTACTACGTGCTTTCTGGTGGCAGCCACCCCTTT GGAGACAGTCTTTATCGCCAGGCAAACATCCTCACAGGGGCTCCCTGTCTGGCTCACCTG GAGGAAGAGGTCCACGACAAGGTGGTTGCCCGGGACCTGGTTGGAGCCATGTTGAGCCCA CTGCCGCAGCCACCCTTTGCCCCCCAGGTGCTGGCCCACCCCTTCTTTTGGAGCAGA GAGCCCCTGGTGAGGGCACTGGAGGCGGGAGGCTGCGCAGTGGTCCGGGACAACTGGCAC GAGCACATCTCCATGCCGCTGCAGACAGATCTGAGAAAGTTCCGGTCCTATAAGGGGACA TCAGTGCGAGACCTGCTCCGTGCTGAGGAACAAGAAGCACCACTACAGGGAGCTCCCA GTTGAGGTGCGACAGGCACTCGGCCAAGTCCCTGATGGCTTCGTCCAGTACTTCACAAAC CGCTTCCCACGGCTGCTCCTCCACACGCACCGAGCCATGAGGAGCTGCGCCTCTGAGAGC CTCTTCCTGCCCTACTACCCGCCAGACTCAGAGGCCAGGAGGCCATGCCCTGGGGCCACA GGGAGGTGA

### SEQ ID NO: 79 HGP 6644466

GGAGGGTTCGAATTGCAACGGCAGCTGCCGGGCGTATGTGTTGGTGCTAGAGGCAGCTGC AGGGTCTCGCTGGGGCCGCTCGGGACCAATTTTGAAGAGGTACTTGGCCACGACTTATT TTCACCTCCGACCTTTCCTTCCAGGCGGTGAGACTCTGGACTGAGAGTGGCTTTCACAAT GGAAGGGATCAGTAATTTCAAGACACCAAGCAAATTATCAGAAAAAAAGAAATCTGTATT ATGTTCAACTCCAACTATAAATATCCCGGCCTCTCCGTTTATGCAGAAGCTTGGCTTTGG TACTGGGGTAAATGTGTACCTAATGAAAAGATCTCCAAGAGGTTTGTCTCATTCTCCTTG GGCTGTAAAAAAGATTAATCCTATATGTAATGATCATTATCGAAGTGTGTATCAAAAGAG ACTAATGGATGAAGCTAAGATTTTGAAAAGCCTTCATCATCCAAACATTGTTGGTTATCG TGCTTTTACTGAAGCCAATGATGGCAGTCTGTGTCTTGCTATGGAATATGGAGGTGAAAA CATAATTTTAAAAGTTGCTTTGAATATGGCAAGAGGGTTAAAGTATCTGCACCAAGAAAA GAAACTGCTTCATGGAGACATAAAGTCTTCAAATGTTGTAATTAAAGGCGATTTTGAAAC AATTAAAATCTGTGATGTAGGAGTCTCTCTACCACTGGATGAAAATATGACTGTGACTGA CCCTGAGGCTTGTTACATTGGCACAGAGCCATGGAAACCCAAAGAAGCTGTGGAGGAGAA TGGTGTTATTACTGACAAGGCAGACATATTTGCCTTTGGCCTTACTTTGTGGGAAATGAT GACTTTATCGATTCCACACATTAATCTTTCAAATGATGATGATGATGAAGATAAAACTTT TGATGAAAGTGATTTTGATGATGAAGCATACTATGCAGCGTTGGGAACTAGGCCACCTAT TAATATGGAAGAACTGGATGAATCATACCAGAAAGTAATTGAACTCTTCTCTGTATGCAC



#### FIGURE 2MMM

SEQ ID NO: 80 AA449542 M ATCTCCAAGAGGGTTGTCTCATTCTCCTTGGGCCGTGAAAAAGATAAGTCTTTTATGCGA TGATCATTATCGAACTGTGTATCAGAAGAGACTAACTGATGAAGCTAAGATTTTAAAAAA CCTTAATCACCCAAACATTATAGGATATCGTGCTTTTACTGAAGCCAGTGATGGTAGTCT GTGCCTTGCTATGGAGTATGGAGGTGAAAAGTCTCTGAATGACTTAATAGAAGAGCGGAA CAAAGACAGTGGAAGTCCTTTTCCAGCAGCTGTAATTCTCAGAGTTGCTTTGCACATGGC CAGAGGGCTAAAGTACCTGCACCAAGAAAAGAAGCTGCTTCATGGAGACATAAAGTCTTC AAATGTTGTAATTAAAGGTGATTTTGAAACAATTAAAATCTGTGATGTAGGAGTCTCTCT GCCATTGGATGAAAATATGACTGTGACTGATCCTGAGGCCTGTTATATTGGTACTGAGCC ATGGAAACCCAAGGAAGCGTTGGAAGAAAATGGCATCATTACTGACAAGGCAGATGTGTT TGCTTTTGGCCTTACTCTGTGGGAAATGATGACTTTATGTATTCCACACGTCAATCTTCC AGATGATGATGATGAAGATGCAACCTTTGATGAGAGTGACTTCGATGATGAAGCATA TTATGCAGCTCTGGGGACAAGGCCATCCATCAACATGGAAGAGCTGGATGACTCCTACCA GAAGGCCATTGAACTCTTCTGTGTGTGCACTAATGAGGATCCTAAAGATCGCCCGTCTGC TGCACACATCGTTGAAGCTTTGGAACTAGATGGCCAATGTTGTGGTCTAAGCTCAAAGCA TTAACTTGTATGGGAACTGTTAACTAGATATATGTAGTTAATATAACTTATGGTAGCTAG ATTCTAGAAGTAGCTTTAACACTAGTGACCCCTGTCTAAGATGACTTAAGAATCAAGGGA CCATTGCTTTGTTACAGATCTTTTTAGATATTCTTGCTTCTTTAGTGGGTTACTAAAAAT TTCACTACGTACATGTGGTACAGATATCTGTCTGCTCATAGTGTCAGTCCTTCAGCTGGC CTGTCAGCCCATGCGCCCTGGGACTTGAGAAGAGTTCATAAACGTAGCTCCTAGGGTGTC TTGCCTCTCTACACTTAGCTTCTAATTTATTACTTTGTTTCTACTGATTGTGTCTTAAGT

CTTTTAAAATAAATGTAAGAATAAACAATAAAAGACAGTTTTAGTACCAGG

SEQ ID NO: 82\_AA232253\_H
ATGTCGTCTCTCGGTGCCTCCTTTGTGCAAATTAAATTTGATGACTTGCAGTTTTTTGAA
AACTGCGGTGGAGGAAGTTTTGGGAGTGTTTATCGAGCCAAATGGATATCACAGGACAAG
GAGGTGGCTGTAAAGAAGCTCCTCAAAATAGAGAAAGAGGCAGAAATACTCAGTGTCCTC
AGTCACAGAAACATCATCCAGTTTTATGGAGTAATTCTTGAACCTCCCAACTATGGCATT
GTCACAGAATATGCTTCTCTGGGATCACTCTATGATTACATTAACAGTAACAGAAGTGAG
GAGATGGATATGGATCACATTATGACCTGGGCCACTGATGTAGCCAAAGGAATGCATTAT
TTACATATGGAGGCTCCTGTCAAGGTGATTCACAGAGACCTCAAGTCAAGAAACGTTGTT

WO 00/73469 PCT/US00/14842

### **FIGURE 2NNN**

ATAGCTGCTGATGGAGTATTGAAGATCTGTGACTTTGGTGCCTCTCGGTTCCATAACCAT CTCCCTGTGTCAGAAACTTGTGACACATATTCCTATGGTGTGGTTCTCTGGGAGATGCTA ACAAGGGAGGTCCCCTTTAAAGGTTTGGAAGGATTACAAGTAGCTTGGCTTGTAGTGGAA AAAAACGAGAGATTAACCATTCCAAGCAGTTGCCCCAGAAGTTTTGCTGAACTGTTACAT CAGTGTTGGGAAGCTGATGCCAAGAAACGGCCATCATTCAAGCAAATCATTTCAATCCTG GAGTCCATGTCAAATGACACGAGCCTTCCTGACAAGTGTAACTCATTCCTACACAACAAG GCGGAGTGGAGGTGCGAAATTGAGGCAACTCTTGAGAGGCTAAAGAAACTAGAGCGTGAT CTCAGCTTTAAGGAGCAGGAGCTTAAAGAACGAGAAAGACGTTTAAAGATGTGGGAGCAA GAAGACGATGTGTATTGGTGGGTTCAGCAGCTCGTCAGAAAAGGTGACTCTTCAGCAGAG ATGAGTGTATATGCAAGCTTGTTTAAAGAAAACAACATTACAGGGAAGCGGCTGCTGCTG CTGGAGGAAGACCTGAAAGACATGGGCATTGTCTCCAAGGGGCATATCATTCACTTC AAGTCAGCCATTGAGAAATTAACCCATGATTACATAAATTTGTTTCACTTCCCACCACTA ATTAAGGACTCAGGAGGTGAACCTGAAGAAAATGAGGAAAAAATAGTGAACCTGGAACTG GTTTTTGGTTTTCACTTGAAACCAGGAACTGGCCCACAGGATTGTAAGTGGAAAATGTAT ATGGAGATGGATGGGGATGAAATTGCAATAACCTACATAAAAGATGTGACATTCAACACT AACCTACCTGATGCGGAGATTTTAAAGATGACAAAGCCACCATTTGTAATGGAGAAGTGG ATTGTAGGAATAGCAAAAAGTCAGACTGTGGAGTGCACTGTCACATATGAGAGTGATGTT AGAACTCCAAAAAGCACTAAACATGTCCATTTGATTCAGTGGAGTAGAACAAAACCTCAG GATGAAGTGAAAGCAGTCCAACTTGCCATTCAGACATTATTCACCAATTCAGATGGCAAC CCTGGAAGCAGGTCCGACTCAAGTGCTGATTGCCAGTGGTTAGATACTCTGAGGATGCGG CAGATTGCATCCAACACTTCTTTACAGCGTTCCCAGAGCAATCCTATTCTGGGGTCACCG TTCTTCTCACACTTTGATGGCCAGGATTCCTACGCTGCTGCTGTGAGACGGCCCCAGGTG CCCATTAAGTATCAACAGATTACACCTGTGAACCAGTCCAGAAGCTCGTCTCCTACTCAG TATGGACTGACCAAAAACTTCTCTTCCTTACATCTCAACTCTAGGGACAGTGGCTTTTCC TATGGACGTGGTAGTATATCACTCAATTCTTCTCCTAGAGGAAGATACAGTGGAAAGAGT CAGCATTCCACTCCATCAAGAGGAAGATACCCTGGAAAGTTCTACAGGGTTTCTCAGTCA GCACTCAATCCTCACCAGTCGCCTGACTTCAAGAGAAGCCCCAGGGACCTCCACCAACCC AGCAAAGTCAGCGAAGGGGGCTGGACAAAAGTGGAATACCGGAAAAAGCCCCCACAGGCCA TGA

SEQ ID NO: 83 AI375137 H

ATGGGAAATTATAAATCTAGACCAACCCAAACTTGTACTGATGAATGGAAGAAAAAAGTC AGTGAATCATATGTTATCACAATAGAAAGATTAGAAGATGACCTGCAGATCAAGGAAAAA GAACTGACAGAACTAAGGAATATATTTGGCTCTGATGAAGCCTTCAGTAAAGTCAATTTA AATTACCGCACTGAAAATGGGCTGTCTCTACTTCATTTATGTTGCATTTGTGGAGGCAAG AAATCACATATTCGAACTCTTATGTTGAAAGGGCTCCGCCCATCTCGACTGACAAGAAAT GGATTTACAGCCTTGCATTTAGCAGTTTACAAGGATAATGCAGAATTGATCACTTCTCTG CTTCACAGTGGAGCTGATATACAGCAGGTTGGATACGGTGGCCTCACTGCCCTCCATATT GCTACAATAGCTGGCCACCTAGAGGCTGCTGATGTGCTGTTGCAACATGGAGCTAATGTC AATATTCAAGATGCAGTTTTTTTCACTCCATTGCATATTGCAGCGTACTATGGACATGAA CAGGTAACTCGCCTTCTTTTGAAATTTGGTGCTGATGTAAATGTAAGTGGTGAAGTTGGA GATAGACCCCTCCACCTAGCATCTGCAAAAGGATTCTTGAATATTGCAAAACTCTTGATG GAAGAAGCCAGCAAAGCAGATGTGAATGCTCAAGATAATGAAGACCATGTCCCACTCCAT TTCTGTTCTCGATTTGGACACCATGATATAGTTAAGTATCTGCTGCAAAGTGATTTGGAA GTTCAACCTCATGTTGTTAATATCTATGGAGATACCCCCTTACACCTGGCATGCTACAAT WO 00/73469 PCT/US00/14842

# **FIGURE 2000**

GGCAAATTTGAAGTTGCCAAGGAAATCATCCAAATATCAGGAACAGAAAGTCTGACTAAG GAAAACATCTTCAGTGAAACAGCTTTTCATAGTGCTTGTACCTATGGCAAGAGCATTGAC CACACTGGATTACACTCTGCTTGCTACCACGGTCACATTCGCCTGGTTCAGTTCTTACTG GATAATGGAGCTGATATGAATCTAGTGGCTTGTGATCCCAGCAGGTCTAGTGGTGAAAAA GATGAGCAGACATGTTTGATGTGGGCTTATGAAAAAGGGCATGATGCCATTGTCACACTC CTGAAGCATTATAAGAGACCACAAGATGAATTGCCCTGTAATGAATATTCTCAGCCTGGA GGAGATGGCTCCTATGTGTCTGTTCCATCACCCTTGGGGAAGATTAAAAGCATGACAAAA GAGAAGGCAGATATTCTCCTCCTAAGAGCTGGATTGCCTTCACATTTCCATCTTCAGCTC TCAGAAATTGAGTTCCATGAGATTATTGGCTCAGGTTCTTTTGGGAAAGTATATAAAGGA CGATGCAGAAATAAAATAGTGGCTATAAAACGTTATCGAGCCAATACCTACTGCTCCAAG TCAGATGTGGATATGTTTTGCCGAGAGGTGTCCATTCTCTGCCAGCTCAATCATCCCTGC TACATATCAGGGGGTTCTCTGTTCTCCCTCCTTCATGAGCAGAAGAGGATTCTTGATTTG CAGTCTAAATTAATTATTGCAGTAGATGTTGCCAAAGGCATGGAGTACCTTCACAACCTG ACACAGCCAATTATACATCGTGACTTGAACAGTCACAATATTCTTCTCTATGAGGATGGG CATGCTGTGGTGGCAGATTTTGGAGAATCAAGATTTCTACAGTCTCTGGATGAAGACAAC ATGACAAACAACCTGGGAACCTCCGTTGGATGGCTCCTGAGGTGTTCACGCAGTGCACT GGCGAAATTCCATTCGCTCATCTCAAGCCAGCGGCTGCGGCAGCAGACATGGCTTACCAC CACATCAGACCTCCCATTGGCTATTCCATTCCCAAGCCCATATCATCTCTGCTGATACGA GGGTGGAACGCATGTCCTGAAGGAAGACCCGAATTTTCTGAAGTTGTCATGAAGTTAGAA GAGTGTCTCTGCAACATTGAGCTGATGTCTCCTGCATCAAGTAACAGCAGTGGGTCTCTC TCACCTTCTTCTTCTGATTGCCTGGTGAACCGGGGAGGACCTGGCCGGAGTCATGTG GCAGCATTAAGAAGTCGTTTCGAATTGGAATATGCTCTAAATGCAAGGTCCTATGCTGCT AGTCTTCAATACACCCCATTGACAAATATGGCTATGTATCCGATCCCATGAGCTCAATG CATTTCATTCTTGCCGAAATAGTAGCAGCTTTGAGGACAGCAGCTGA

### SEQ ID NO: 84 H97685 H

ATGATTTCTTGCCTGTNATAACCTATGCACTCACAAAGATGAACTCTCTGAGAGGGATGA GCAAGAGCTTCAGGAAATCCGAAAGTATTTCTCCTTTTCCTGTATTCTTTTTCAAAGTGCC GAAACTGGGCTCGGAGATAATAGACTCCTCAACCAGGAGAATGGAGAGCGAAAGATCACC GCTTTATCGCCAGCTAATTGACCTGGGCTATCTGAGCAGCAGTCACTGGAACTGTGGGGC TCCTGGCCAGGATACTAAAGCTCAGAGCATGTTGGTGGAACAGAGTGAAAAGCTGAGACA CTTGAGCACATTTTCTCACCAGGTGTTACAGACTCGCCTGGTGGATGCAGCCAAGGCCCT GAACCTGGTGCACTGCCTTGACATCTTTATTAACCAGGCATTTGACATGCAGCG GGACCTGCAGATCACTCCCAAACGTCTGGAATATACTCGAAAAAAGGAGAATGAGTTGTA TGAATCATTGATGAATATTGCCAACCGAAAGCAGGAGGAAATGAAGGATATGATTGTTGA GACACTTAATACCATGAAGGAGGAACTTCTGGATGATGCTACTAACATGGAGTTTAAAGA CGTCATTGTCCCTGAGAATGGAGAACCAGTAGGCACCAGAGAGATCAAATGCTGCATCCG ACAGATCCAGGAACTCATCATCTCCCGACTTAATCAGGCAGTGGCTAATAAGCTGATCAG CTCAGTGGATTACCTGAGGGAAAGCTTCGTCGGAACCCTGGAACGATGTCTGCAGAGCCT GGAGAAGTCTCAGGATGTCTCAGTTCACATCACCAGTAATTATCTCAAACAGATCTTAAA TGCTGCCTATCATGTTGAAGTCACGTTTCACTCAGGGTCGTCAGTTACAAGGATGCTATG GGAGCAAATCAAACAGATCATCCAGCGCATCACATGGGTGAGCCCACCTGCCATCACTCT GGAATGGAAGAGGAAGCCCAGGAAGCCATTGAGAGCCTCAGCGCCTCCAAATTGGC TAAGAGCATTTGCAGCCAATTCCGGACTCGGCTCAATAGTTCCCACGAGGCTTTTGCAGC CTCCTTGCGGCAGCTGGAAGCTGGCCACTCAGGCCGGTTAGAGAAAACGGAAGATCTATG GCTGAGGGTTCGGAAAGATCATGCTCCCCGCCTGGCCCGCCTTTCTCTGGAAAGCCGTTC

### FIGURE 2PPP

TTTACAGGATGTCTTGCTTCATCGTAAACCTAAACTGGGACAGGAACTGGGCCGGGGCCA GTATGGTGTGTATACCTGTGTGACAACTGGGGAGGACACTTCCCTTGTGCCCTCAAATC AGTTGTCCCTCCAGATGAGAAGCACTGGAATGATCTGGCTTTGGAATTTCACTATATGAG GTCTCTGCCGAAGCATGAGCGATTGGTGGATCTCCATGGTTCAGTCATTGACTACAACTA TGGTGGTGCTCCAGCATTGCTGTGCTCCTCATTATGGAGCGGCTACACCGGGATCTCTA CACAGGGCTGAAGGCTGACCCTGGAGACACGTTTGCAGATAGCACTAGATGTGGT GGAGGGAATCCGCTTCCTGCACAGCCAGGGACTTGTCCATCGTGATATCAAACTGAAAAA TGTGCTGCTGGATAAGCAGAACCGTGCCAAGATCACTGACTTAGGATTCTGCAAGCCAGA GGCCATGATGTCAGGCAGCATTGTGGGGGACACCAATCCATATGGCCCCTGAACTTTTCAC AGGGAAGTACGATAATTCCGTGGATGTCTACGCTTTTGGAATTCTTTTCTGGTATATCTG CTCAGGCTCTGTCAAGCTCCCTGAGGCATTTGAGAGGTGTGCTAGCAAAGACCATCTCTG GAACAATGTGCGGAGGGGGCTCGCCCAGAACGTCTTCCTGTGTTTGATGAGGAGTGCTG GCAGTTGATGGAAGCCTGTTGGGATGGCGACCCCTTGAAGAGGCCTCTCTTGGGCATTGT CCAGCCCATGCTCCAGGGCATCATGAATCGGCTCTGCAAGTCCAATTCTGAGCAGCCAAA CAGAGGACTAGATGATTCTACTTGAAAGCAAAGACCTTTCTCTTTCACTCTAGTTATT TCCTTCCCCCTCACCATTTGGCCATGGGGAGAATTTGACATTTATTCACTATAGGACACA TGGACAGTGAAGAGTTGAATGACTGAGCATATTCAGCAGCTCACTGAAGCGCCAAGCTAT CCCTTTAGCAAAAAGTGTCTCAGATGTGTAAAAGCTGAGGAATGTGGTGTTCTGGCTTC ACAAATGAAAAGGAGGCAGATGTT

# SEQ ID NO: 85\_W20810\_M

TTGATGTCAACCTGAAGGCTTCTAAAGCGAGTGATGTCTACAGCTTTGGGATCCTCGTGT GGGCAGTGCTGGCTGGCAGAGAGCTGAGTTGGTAGACAAGACTTCACTAATCCGGGAAA CAGTGTGTGACAGGCAGAGTCGTCCTCCACTGACAGAGCTGCCTCCAGGTAGCCCTGAGA CTCCCGGCTTGGAAAAACTGAAGGAGTTAATGATTCATTGCTGGGGTTCCCAGTCCGAAA ACAGGCCATCCTTCCAGGACTGCGAACCAAAAACCAATGAAGTTTACAATCTGGTAAAGG ACAAGGTAGATGCTGCTGTCTCCGAGGTAAAGCATTATCTGTCTCAGCACAGAAGCAGCG GCAGAAACTTGTCTGCCAGAGAGCCAAGCCAAAGAGGCACAGAAATGGATTGCCCGAGGG AAACCATGGTTTCTAAAATGCTGGACCGCCTGCATTTGGAGGAACCCTCCGGACCAGTTC CTGGAAAATGTCCTGAGAGGCAAGCACAGGACACATCAGTTGGGCCTGCCACACCAGCAA GGACATCTTCTGACCCCGTGGCTGGCACTCCTCAGATTCCACATACTTTACCCTTCAGAG GCACAACACCTGGGCCAGTCTTTACTGAGACTCCCGGTCCTCACCCCCAAAGGAATCAGG GAGATGGAAGACACGGCACTCCTTGGTATCCCTGGACCCCACCGAATCCAATGACAGGGC CACCGGCTCTCGTCTTCAACAACTGTTCTGAAGTGCAGATTGGGAACTACAACTCCTTGG TAGCACCACCAAGAACTACTGCCTCAAGTTCGGCCAAGTATGACCAAGCACAGTTCGGCA GGGGTAGGGCTGGCAGCCCTTCCACAAGTAGACTTCAGAGAATCACTGCAAGAGCCTGA AGTGTGCCATTCAGCGTGGCAATAAAAAGCACGTTTTAAGCAACCTGGACTGGCTAAGAC AGTCCTTGCCACTTCCTGAAGCTCACAACATTCTGTGAGGACAGTTGGACCTACACCCAA ACTGACTCTTGACCCATCTCCTTAAAGTCAATAAACATAGCATGTTAACTGTG

# SEQ ID NO: 86 AA744236 H



## FIGURE 2000

CAGTCAATAAGAGACCCAGCATCTATCCCTCCTGAAGAGATGTCTCCAGAATTCACAACT CTCCCAGAGTGTCATGGACATGCCCGGGATGCCTTTTCATTTGGAACATTGGTGGAAAGT TTGCTCACAATCTTAAATGAACAGGTTTCAGCGGATGTTCTCCCAGCTTTCAACAGACC TTGCACTCAACTTTGCTGAATCCCATTCCAAAATGTCGGCCAGCGCTCTGCACCTTACTA TCTCATGACTTCTTCAGAAATGATTTTCTGGAAGTTGTGAATTTCTTGAAAAGTTTAACA TTGAAGAGTGAAGAGGAGAAAACGGAATTCTTTAAATTTCTGCTGGACAGAGTCAGCTGC TTGTCAGAGGAATTGATAGCTTCAAGGTTGGTGCCTCTTCTGCTTAATCAGTTGGTGTTT GCAGAGCCAGTGGCTGTTAAGAGTTTTCTTCCTTATCTGCTTGGCCCCAAAAAAGATCAT GCGCAGGGAGAAACTCCTTGCTTGCTCTCACCAGCCCTGTTCCAGTCACGGGTGATCCCC GTGCTTCTCCAGTTGTTTGAAGTTCATGAAGAGCATGTGCGGATGGTGCTGCTGTCTCAC ATCGAGGCCTACGTGGAGCACTTCACTCAGGAGCAGCTGAAGAAAGTCATCTTGCCACAG GTTTTGCTGGGCCTGCGTGATACTAGCGATTCCATTGTGGCAATTACTCTGCATAGCCTA TTCAAACGCACTGCCCCAAGTTTTACTAAAAATACTGACCTTTCTCTAGAAGGCGATCCA TTTTCTCAGCCTATTAAATTTCCCATAAATGGACTCTCAGATGTAAAAAATACTTCGGAG GACAGTGAAAACTTCCCATCAAGTTCTAAAAAGTCTGAGGAGTGGCCTGACTGGAGTGAA CCTGAGGAGCCTGAAAATCAAACTGTCAACATACAGATTTGGCCTAGAGAACCTTGTGAT GATGTCAAGTCCCAGTGCACTACCTTGGATGTGGAAGAGTCATCTTGGGATGACTGCGAG CCCAGCAGCTTAGATACTAAAGTAAACCCAGGAGGTGGAATCACTGCTACAAAACCTGTT TGGAAATCAAGCTTACCCCAAAAGATTAGCCTTGTACAAAGGGGGGGATGACGCAGACCAA ATCGAGCCGCCAAAAGTGTCATCACAAGAAAGGCCCCTTAAGGTTCCATCAGAACTTGGT TTAGGAGAGGAATTCACCATTCAAGTAAAAAAGAAGCCAGTAAAAGATCCTGAGATGGAT TGGTTTGCTGATATGATCCCAGAAATTAAGCCTTCTGCTGCTTTTCTTATATTACCTGAA CTGAGGACAGAAATGGTCCCAAAAAAGGATGATGTCTCCCCAGTGATGCAGTTTTCCTCA <u>AAATTTGCTGCAGCAGAAATTACTGAGGGAGAGGCTGAAGGCTGGGAAGAAGAAGGGGGA</u> CTGAACTGGGAAGATAATAACTGGTGA

SEQ ID NO: 87 AI052250 H

AGCGGCCGCGGGGCGGCGGAGGATATGGAGTAAAGCCAGAGTCAGTGGCCAGGCACGAA CCGCCCTCCTGGAAGAAGGAAGGTAACTATAACTACCCAATATTGCAGCCATGGAGT CCATGCTTAATAAATTGAAGAGTACTGTTACAAAAGTCACAGCTGATGTCACTAGTGCGG TAATGGGAATTCCTGTCACTAGAGAATTTGATGTTGGTCGACACATTGCCAGTGGT<u>TGC</u>A ATGGGCTAGCTTGGAAGATTTTTAATGGCACAAAAAAGTCAACAAAGCAGGAAGTGGCAG TTTTTGTCTTTGATAAAAAACTGATTGACAAGTATCAAAAATTTGAAAAGGATCAAATCA TTGATTCTCTAAAACGAGGAGTCCAACAGTTAACTCGGCTTCGACACCCTCGACTTCTTA CTGTCCAGCATCCTTTAGAAGAATCCAGGGATTGCTTGGCATTTTGTACAGAACCAGTTT TTGCCAGTTTAGCCAATGTTCTTGGTAACTGGGAAAATCTACCTTCCCCTATATCTCCAG ACATTAAGGATTATAAACTTTATGATGTAGAAACCAAATATGGTTTGCTTCAGGTTTCTG AAGGATTGTCATTCTTGCATAGCAGTGTGAAAATGGTGCATGGAAATATCACTCCTGAAA ATATATTTTGAATAAAAGTGGAGCCTGGAAAATAATGGGTTTTGATTTTTGTGTATCAT CAACCAATCCTTCTGAACAAGAGCCTAAATTTCCTTGTAAAGAATGGGACCCAAATTTAC GGAAACCTATATTTGAAGTCAACAAGCAAGATATTTACAAGAGTTTCAGTAGGCAGTTGG ATCAGTTGAGTCGTTTAGGATCTAGTTCACTTACAAATATACCTGAGGAAGTTCGTGAAC ATGTAAAGCTACTGTTAAATGTAACTCCGACTGTAAGACCAGATGCAGATCAAATGACAA AGATTCCCTTCTTTGATGATGTTGGTGCAGTAACACTGCAATATTTTGATACCTTATTCC AAAGAGATAATCTTCAGAAATCACAGTTTTTCAAAGGACTGCCAAAGGTTCTACCAAAAC WO 00/73469 PCT/US00/14842

### FIGURE 2RRR

SEQ ID NO: 88 AA278842 H GGCGCCCAGATATCACACGTGCCAAGGGGCTGGCTCAGCCCCGGCTCGGGCGGCGGAG GACCCGGAGCTAAGGCGCCCGAACCCGCGGCGGCGGTGGGGACGATGTGGTTCTTTGCCC GGGACCCGGTCCGGGACTTTCCGTTCGAGCTCATCCCGGAGCCCCCAGAGGGCGGCCTGC CCGGGCCCTGGGCCTGCACCGCGGCCGCAAGAAGGCCACAGGCAGCCCCGTGTCCATCT TCGTCTATGATGTGAAGCCTGGCGCGGAAGAGCAGACCCAGGTGGCCAAAGCTGCCTTCA AGCGCTTCAAAACTCTACGGCACCCCAACATCCTGGCTTACATCGATGGACTGGAGACAG AAAAATGCCTCCACGTCGTGACAGAGGCTGTGACCCCGTTGGGAATATACCTCAAGGCGA GAGTGGAGGCTGGTGGCCTGAAGGAGCTGGAGATCTCCTGGGGGCTACACCAGATCGTGA AAGCCCTCAGCTTCCTGGTCAACGACTGCAGCCTCATCCACAACAATGTCTGCATGGCCG CCGTGTTCGTGGACCGAGCTGGCGAGTGGAAGCTTGGGGGCCTGGACTACATGTATTCGG CCCAGGGCAACGGTGGGGGACCTCCCCGCAAGGGGATCCCCGAGCTTGAGCAGTATGACC GGCGCTTGGGCTGCCTCATTTGGGAAGTCTTCAATGGGCCCCTACCTCGGGCAGCAGCCC TACGCAACCCTGGGAAGATCCCCAAAACGCTGGTGCCCCATTACTGTGAGCTGGTGGGAG CAAACCCCAAGGTGCGTCCCAACCCAGCCGGTTCCTGCAGAACTGCCGGGCACCTGGTG GCTTCATGAGCAACCGCTTTGTAGAAACCAACCTCTTCCTGGAGGAGATTCAGATCAAAG AGCCAGCCGAGAAGCAAAAATTCTTCCAGGAGCTGAGCAAGAGCCTGGACGCATTCCCTG AGGATTTCTGTCGGCACAAGGTGCTGCCCCAGCTGCTGACCGCCTTCGAGTTCGGCAATG CTGGGGCCGTTGTCCTCACGCCCCTCTTCAAGGTGGGCAAGTTCCTGAGCGCTGAGGAGT ATCAGCAGAAGATCATCCCTGTGGTGGTCAAGATGTTCTCATCCACTGACCGGGCCATGC GCATCCGCCTCCTGCAGCAGATGGAGCAGTTCATCCAGTACCTTGACGAGCCAACAGTCA ACACCCAGATCTTCCCCCACGTCGTACATGGCTTCCTGGACACCCAACCCTGCCATCCGGG AGCAGACGGTCAAGTCCATGCTCCTGGCCCCAAAGCTGAACGAGGCCAACCTCAATG TGGAGCTGATGAAGCACTTTGCACGGCTACAGGCCAAGGATGAACAGGGCCCCATCCGCT GCAACACCACAGTCTGCCTGGGCAAAATCGGCTCCTACCTCAGTGCTAGCACCAGACACA GGGTCCTTACCTCTGCCTTCAGCCGAGCCACTAGGGACCCGTTTGCACCGTCCCGGGTTG CGGGTGTCCTGGGCTTTGCTGCCACCCACAACCTCTACTCAATGAACGACTGTGCCCAGA AGATCCTGCCTGTGCTCTGCGGTCTCACTGTAGATCCTGAGAAATCCGTGCGAGACCAGG CCTTCAAGGCCATTCGGAGCTTCCTGTCCAAATTGGAGTCTGTGTCGGAGGACCCGACCC AGCTGGAGGAAGTGGAGATGTCCATGCAGCCTCCAGCCCTGGCATGGGAGGAGCCG GTTCGCACCCAACCACTGCCCCAACAGAACCCAACATTCCCCAAAGACCCACGCCTGAAG GAGTTCCTGCCCCAGCCCCACCCCTGTTCCTGCCACCCCTACAACCTCAGGCCACTGGG AGACGCAGGAGGAGACAAGGACACAGCAGGACAGCACTGCTGACAGATGGGACG ACGAAGACTGGGGCAGCCTGGAGCAGGAGGCCGAGTCTGTGCTGGCCCAGCAGGACGACT GGAGCACCGGGGGCCAAGTGAGCCGTGCTAGTCAGGTCAGCAACTCCGACCACAAATCCT CCAAATCCCCAGAGTCCGACTGGGAGCCTGGGAAGCTGAGGGCTCCTGGGAACAGGGTT GGCAGGAGCCAAGCTCCCAGGAGCCACCTCCTGACGGTACACGGCTGGCCAGCGAGTATA ACTGGGGTGGCCCAGAGTCCAGCGACAAGGGCGACCCCTTCGCTACCCTGTCTGCACGTC CCAGCACCCAGCCGAGGCCAGACTCTTGGGGTGAGGACAACTGGGAGGGCCTCGAGACTG

#### FIGURE 2SSS

SEQ ID NO: 89 AA599286 H ATGGCCTTCATGGAGAAGCCGCCAGCCGGCAAGGTGCTGCTGGACGACACGGTGCCGCTG ACAGCAGCCATCGAGGCGAGCCAGAGCCTGCAGTCCCACACGGAATATATTATTCGAGTG CAAGGAGGAATTTCTGTGGAAAACAGCTGGCAGATTGTTAGAAGATACAGTGACTTTGAT TTGCTTAACAACAGCTTACAGATTGCAGGCCTAAGTCTACCTCTTCCTCCCAAAAAATTG ATTGGTAACATGGATCGTGAATTCATAGCTGAAAGGCAGAAAGGTCTTCAGAACTATCTC AACGTGATCACAACAAATCATATCTTGTCTAATTGTGAGCTGGTTAAGAAGTTTTTAGAT CCAAACAACTATTCCGCAAACTATACTGAGATTGCCTTGCAACAGGTTTCCATGTTCTTC CGATCAGAGCCAAAGTGGGAGGTGGTGGAACCTTTGAAAGACATAGGTTGGAGAATAAGG AAGAAATATTTCTTGATGAAGATTAAAAATCAGCCAAAGGAACGGCTAGTGTTAAGCTGG GCTGACCTTGGCCCAGACAAGTATTTGTCAGATAAAGATTTTCAGTGTCTAATCAAACTT CTGCCTTCTTGTTTGCACCCTTACATCTATCGGGTTACCTTTGCCACAGCTAATGAATCC TCAGCGTTGCTAATTAGGATGTTTAACGAAAAGGGAACATTGAAGGATCTGATCTACAAG GCAAAACCAAAAGACCCATTTCTAAAGAAGTACTGCAACCCTAAGAAGATTCAGGGCCTG GAACTCCAGCAAATAAAAACATATGGACGGCAAATATTAGAGGTACTGAAGTTTCTTCAT GACAAGGGATTCCCTTATGGGCATCTTCACGCCTCCAATGTGATGCTCGATGGGGACACT TTTTCACAATTCAGGAAAATCAATACATTGGAAAGTGTGGATGTCCACTGCTTTGGCCAC TTACTGTATGAAATGACTTATGGACGACCGCCAGACTCGGTGCCTGTGGACTCCTTCCCT CCTGCCCGTCCATGGCTGTGGTGGCCGTGTTGGAGTCTACGCTGTCTTGTGAAGCCTGT AAAAATGGCATGCCTACCATCTCCCGGCTCTTACAGATGCCATTATTCAGCGATGTTTTA CTAACCACTTCTGAAAAACCACAGTTTAAGATCCCTACAAAGTTAAAAGAGGCATTGAGA ATTGCCAAAGAATGTATAGAGAAGAGACTAATTGAGGAACAGAAACAGATTCACCAGCAT ATTTTAGCTCGAAAGAAGTCAAAACGATCTGCTCTTGAAAATAGTGAAGAGCATTCAGCG AAGTACAGCAACTCCAATAATTCAGCAGGATCTGGGGCCAGCTCACCTCTCACGTCCCCG TCATCGCCAACTCCACCCTCTACATCAGGGATATCTGCATTACCTCCACCTCCCACCT CCACCACCAGCAGCTCCCTTGCCTCCGAGCACCGAGGCACCTGCCCAGCTCTCG AAAGGAACTTTGAGGAAAGCCAAACCTGTGATCACAGTGCTCCGAAGATCGGCTGAAGCT TCCTGTTTACACTTGGAGGGAAAAGTTCTTTTTTTTTTCCTACTCACCCCTACCCCCAAC TACCCTCTTCCTGGGAAAGTAATTGCTGAGCCAGTACAGCCACAAACAGTACTATTTTGC AGATGCTCATGTAAGCAGCTTTTCGAGAGAAATAATTCTTTAAGCAGAATAAAGTTAGGC TGGCATGCAAAAAAAAAAAAAAAAAAAAAAAA

#### FIGURE 2TTT

TGCATGGTGCTGGAGGTGCTGGGCCACCAGCTCCTCAAATGGATCATCAAGTCCAACTAC CAGGGCCTGCCCTGCGTGAAGAGCATCGTGAGGCAGGTGCTGCACGGCCTGGAC TACCTCCACACCAAGTGCAAGATCATCCACACGGACATCAAGCCCGAGAACATCTTGCTG TGTGTGGGGGACGCTTACATCAGGCGCCTGGCTGCCGAGGCCACGGAGTGGCAACAGGCA GGGGCGCCCCCCCCCCCATAGTCAGCACTGCCCCCAGGAGGTCTTGACCGGT AAGCTGTCCAAAAACAAGAGGAAGAAGATGAGGCGCAAACGGAAACAGCAGAAGCGGCTG CTGGAGGAGCGGCTGCAGAGGCTGGAGGCCATGGAGGCTGCCACCCAGGCT GAGGACTCTGGCTTGAGACTAGACGGGGGCAGCGGCTCCACATCCTCTTCAGGCTTCTCC GGCTCCTCTTCTCCTGCCTCCTGCTCCATCCTCTCCGGCTCGTCCAATCAGCGAGAG ACCGGGGCCTCCTGTCGCCTAGCACCATTCGGTGCCTCGAACCTCCTGGTGAACCCC CTGGAGCCCCAAAATGCAGATAAGATCAAGATCAAGATCGCAGACCTGGGCAACGCCTGC TGGGTGCACAAGCACTTCACGGAAGACATCCAGACTCGGCAGTACCGGGCCGTCGAGGTG  $\tt CTGATCGGCGCCGAATACGGCCCCCCGGCAGACATCTGGAGCACAGCCTGCATGGCCTTC$ GAGCTGGCCACTGGTGACTACCTGTTCGAGCCGCATTCTGGAGAAGACTACAGTCGTGAT GAGGACCACATCGCTCACATAGTGGAGCTTCTGGGGGACATCCCCCCAGCCTTCGCCCTC TCAGGCCGCTATTCCCGGGAGTTCTTCAACCGGAGAGGAGAGCTGCGGCACATCCACAAT CTCAAGCACTGGGGCCTGTACGAGGTACTCATGGAAAAGTACGAGTGGCCCCTAGAGCAG GCCACACAGTTCAGCGCCTTTCTGCTGCCCATGATGGAGTACATCCCCGAAAAGCGGGCC AGTGCCGCTGACTGCCTCCAGCACCCCTGGCTCAACCCCTAG

SEQ ID NO: 91 SGK022 H

GGGGGCGCTGCGATGAAGTCCTTGGGGAGAAAAGGAGCAGGCCAAGGGCGATGGTGGA GTAGAGCTGCCTCTCAGAGGCAGCATGAGCTGAGAGGGTGATAGGAAGGCGGCGCTAGAC AGCATGGAGGACTTTCTGCTCTCCAATGGGTACCAGCTGGGCAAGACCATTGGGGAAGGG ACCTACTCAAAAGTCAAAGAAGCATTTTCCAAAAAACACCAAAGAAAAGTGGCAATTAAA CAAATCGTCCGTACCCTGGACCACAAGAACATCATCCAGGTGTATGAGATGCTGGAGTCT GTGCTGAATGGGGGGCCACTGCCTGAAAGCCGGGCCAAGGCCCTCTTCCGTCAGATGGTT GAGGCCATCCGCTACTGCCATGGCTGTGGTGGCCCACCGGGACCTCAAATGTGAGAAC GCCTTGTTGCAGGGCTTCAACCTGAAGCTGACTGACTTTGGCTTTGCCAAGGTGTTGCCC AAGTCACACCGGGAGCTGAGCCAGACCTTCTGCGGCAGTACAGCCTATGCTGCCCCCGAG GTGCTGCAGGGCATTCCCCACGATAGCAAAAAAGGTGATGTCTGGAGCATGGGTGTGGTC CTGTATGTCATGCTCTGTGCCAGCCTACCTTTTGACGACACAGACATCCCCAAGATGCTG TGGCAGCAGCAGAAGGGGGTGTCCTTCCCCACTCATCTGAGCATCTCGGCCGATTGCCAG GACCTGCTCAAGAGGCTCCTGGAACCCGATATGATCCTCCGGCCTTCAATTGAAGAAGTT AGTTGGCATCCATGGCTAGCAAGCACTTGATAAAAGCAATGGCAAGTGCTCTCCAATAAA GTAGGGGGAGAAAGCAAA

SEQ ID NO: 92\_AA060026\_M SGK022\_M

100/113

#### **FIGURE 2**UUU

SEQ ID NO: 93 AA399669 H CTCCCAAAGTGCTGGGATTACAGGCGTGAGCCACCGGCCCGGCCGCACTTCATTCTCAA GTTTTGTGGCCAACGATGGATAGGAGGTGGATTGTGATGTATTCGGAACATGGGACCTTG AGGAGTTCCGTAACCAAAAGGAGAAAGTAACAACAGCCAGTGGAGACAAAAAGAACTGCT TCTCTTTCTTTCCCCCTCCAAGTTCCTAGTGGAGGGCTGAGTCCAGCATCCCAGACTCGT GTGACTATATAGGCAAGCATTTGGGGACCTACTTCACTTTGATACCCTAGCCTTCAGCAG CTCAAGGTGTTGGCCTTTGGATAGGAGGCTTCCAAGTAGTAAAGCTCCCTGCTCTCAGCA ATTCCCTCATGGATGAATATGGTTATGAGGTGGGCAAGGCCATTGGCCATGGCTCCTATG GGTCGGTATATGAGGCTTTCTACACAAAGCAGAAGGTTATGGTGGCAGTCAAGATCATCT CAAAGAAGAAGGCCTCTGATGACTATCTTAACAAGTTCCTGCCCCGTGAAATACAGGTAA TGAAAGTCTTGCGGCACAAGTACCTCATCAACTTCTATCGGGCCATTGAGAGCACATCTC GAGTATACATCATTCTGGAACTGGCTCAGGGTGGTGATGTCCTTGAATGGATCCAGCGCT ACGGGGCCTGCTCTGAGCCCCTTGCTGGCAAGTGGTTCTCCCAGCTGACCCTGGGCATTG CCTACCTGCACAGCAAGAGCATCGTGCACCGGGACTTAAAGTTGGAGAACCTGTTGCTGG ACAAGTGGGAGAATGTGAAGATATCAGACTTTGGCTTTGCCAAGATGGTGCCTTCTAACC AGCCTGTGGGTTGTAGCCCTKCTTACCGCCAAGTGAACTGCTTTTCCCACCTCAGCCAGA CTTACTGTGGCAGCTTTGCTTACGCTTGCCCAGAGATCTTACGAGGCTTGCCCTACAACC CTTTCCTGTCTGACACCTGGAGCATGGGCGTCATCCTTTACACTCTAGTGGTCGCCCATC TGCCCTTTGATGACACCAATCTCAAAAAGCTGCTAAGAGAGACTCAGAAGGAGGTCACTT TCCCAGCTAACCATACCATCTCCCAGGAGTGCAAGGTCCAACTGCTCATTGCCTGTGTGG CACAATGGAGAAAACTCAGGCAAGACCTCTCTCTCCCCTGCTCTAGAACCTGATCCTCC AGATGCTACGCCAAGCCACTAAGCGTGCCACCATTCTGGACATCATCAAGGATTCCTGGG TGCTCAAGTTCCAGCCTGAGCAACCCACCCATGAGATCAGGCTGCTTGAGGCCATGTGCC AGCTCCACAACACCACTAAACAGCACCAATCCTTGCAAATTACGACCTGAAAATGGCTGA GGGAGGGGGCTAAGAGAGGAGCAAAGCAGGAGGTCTTGGGCTAAAAATCTTTTTTACCAA AAATAAATCTAAGTCTGATTTAGTTTCATCAAAAAAA

WO 00/73469 PCT/US00/14842

#### **FIGURE 2VVV**

CATCATGGTCTGCGGCTCCATGCCCTATGACGACTCCGACATCAGGAAGATGCTGCGTAT
CCAGAAGGAGCACCGTGTGGACTTCCCGCGCTCCAAGAACCTGACCTGCGAGTGCAAGGA
CCTCATCTACCGCATGCTGCAGCCCGACGTCAGCCAGCGGCTCCACATCGATGAGATCCT
CAGCCACTCGTGGCTGCAGCCCCCAAGCCCAAGCCACGTCTTCTGCCTCCTTCAAGAG
GGAGGGGGAGGCCAAGTACCGCGCTGAGTGCAAACTGGACACCAAGACAGGCTTGAGGCC
CGACCACCGGCCCGACCACAAGCTTGGAGCCAAAACCCAGCACCGGCTGCTGGTGGTGCC
CGAGAACGAGAACAGGATGGAGGACAGGCTGGCCGAGACCACCAGGCCCAAAGACCATCA
CATCTCCGGAGCTGAGGTGGGGAAAGCAACCTAGCATGACAATGGCCCCGTTGTGTG
TGGTGGGGGTCGGGGTTGGGGGGCATGGTGCAGTCGGCCTTCACGTAAACTAAGTAGGCA
GGTAGGATCTGAAGAAGGCACAGGTGCAAGTAAAATTCGTCAATTAAACCACTATTTTGA
TT

### SEQ ID NO: 95 AA883975 H

#### SEO ID NO: 96 AA905446 H

CTGGTAGAGAACAGGGCTGGTGCCAAGGCCCATGGAGATGAGAAAACGGAAGACAGGGA TCATGGAAAGAATTGTGGGGTCAGGGGACAGTGGCGGGAGGAGCTGGCTCACCACCCTGT GGACAAATCAGGCCTTATAATTTGTGATTCTGTGGCTTTGTCTAAAAGTCCATAAAGCAC CTTGATATCCAGTCTCACAGACTGCTCACAACAGTCCACAAGGCTGGTGGGGGAGTGCTTC TTTTGAATGATATACTAACGACAAAAATAATAGAAGTGAACATTCTTTGCAATGTCCAAG CAGCTAGACACACTTAAGACCATTAAGAAAGCCAAGAAATAAGACCCAGACAAGGTGGGC AGAAGTTGGAAGGCAGGAGACAGGTGTGAGGAGGTGGGCCTTTCTGATCTGCCAGCCCAT CGTCCGTACCCTGGACCACAAGAACATCATCCAGGTGTATGAGATGCTGGAGTCTGCCGA GAATGGGGGCCACTGCCTGAAAGCCGGGCCAAGGCCCTCTTCCGTCAGATGGTTGAGGC CATCCGCTACTGCCATGGCTGTGGTGGCCCACCGGGACCTCAAATGTGAGAACGCCTT GTTGCAGGGCTTCAACCTGAAGCTGACTGACTTTGGCCTTTGCCAAGGTGTTGCCCAAGTC ACACCGGGAGCTGAGCCAGACCTTCTGCGGCAGTACAGCCTATGCTGCCCCCGAGGTGCT GCAGGGCATTCCCNNCAAGATGCTGTGGCAGCAGCAGAAGGGGGGTGTCCTTCCCCACTCA TCTGAGCATCTCGGCCGATTGCCAGGACCTGCTCAAGAGGCTCCTGGAACCCGATATGAT GCAATGGCAAGTGCTCTCCAATAAAGTAGGGGGAGAAAGCAAACCC

#### FIGURE 2WWW

SEQ ID NO: 97 H29974 H TTACAGCCTGTTGGCGGAGATCGGGCGCGCGCAGCTACGGCGTGGTTTATGAGGCAGTGGC CGGGCGCAGCGGGCCCGGGTGGCGGTCAAGAAGATCCGCTGCGACGCCCCCGAGAACGT GGAGCTGGCGCTGGATTCTGGGCCCTCACCAGCCTCAAGCGGCGCCACCAGAACGT CGTGCAGTTTGAGGAGTGCGTCCTGCAGCGCAATGGGTTAGCCCAGCGCATGAGTCACGG CAACAAGAGCTCGCAGCTTTACCTGCGCCTGGTGGAGACCTCGCTGAAAGGAGAAAGGAT CCTGGGTTATGCTGAGGAGCCCTGCTATCTCTGGTTTGTCATGGAGTTCTGTGAAGGTGG AGACCTGAATCAGTATGTCCTGTCCCGGAGGCCAGACCAGCCACCAACAAAAGTTTCAT GCTACAGCTGACGAGCGCCATTGCCTTCCTGCACAAAAACCATATTGTGCACAGGGACCT GAAGCCAGACAACATCCTCATCACAGAGCGGTCTGGCACCCCCATCCTCAAAGTGGCCGA CTTTGGACTAAGCAAGGTCTGTGCTGGGCTGGCACCCCGAGGCAAAGAGGGCAATCAAGA CAACAAAATGTGAATGAATAAGTACTGGCTGTCCTCAGCCTGCGGTTCGGACTTCTA CATGGCTCCTGAAGTCTGGGAGGGACACTACACAGCCAAGGCGGACATCTTTGCCCTGGG CATTATCATCTGGGCAATGATAGAAAGAATCACTTTTATTGACTCTGAGACCAAGAAGGA GCTCCTGGGGACCTACATTAAACAGGGGACTGAGATCGTCCCTGTTGGTGAGGCGCTGCT AGAAAACCCAAAGATGGAGTTGCACATCCCCCAAAAACGCAGGACTTCCATGTCTGAGGG GATCAAGCAGCTCTTGAAAGATATGTTAGCTGCTAACCCACAGGACCGGCCTGATGCCTT TGAACTTGAAACCAGAATGGACCAGGTCACATGTGCTGCTTAAAATTCAGGGCTAAGCAT TTTGGGTGATTTTAAACTAGGTCGATTCCTCGGGACCCACAGTCTCACCACGTCTCCTCC AGAGGACGGCAGAGGGTACAGGTGGTGGCCTGGCCGGTTGGCGATCTCCCGACAGCTGGA TCCGGCAATGTGAAGCTTTTGTTTGGGTTTCCCCGCTTCTTTTTAGTTTTTGCTTTATTTN TNNCCTTTTCTTTTTTTTTTTTTTCCACNTNCCTTTTTTTAAATTTAAACCATTGAG ACTTCAGAAGAGCAGGACACAATGCTGTGGACAGGCACCAATTTCTTTAAAGAAATTCAA TGTGGGCAAGGCATATGTGTAAATTTCACTTTTACTTTTTATAAGGGGTTAGGGAGCTAT TTTTGGTTTTGTCCTTCACTTTCCCTCTGTCTTCCTTCTTTATACTTTTCTCAGTTCTAC TTATGACACCTCACTTCCCTAGAGAAGGCCTGCCTCCCCATAGGGAATCTGGGGGTANCT TCTGGAACGGGGCGTGAGGANACAAGGAGCCTCTGGGCCACNCCTCCCTACCAGATGCAG GAACTCCTGGACTCCTTGGTGGGCTGGCCCTGGCTAGCCCTTGGGCCTCGGAGATGATCA GAGGTGAAGAACCGCC

SEO ID NO: 98 AA498104 M H29974 M CCGTTGCTGCTCCCCCCCCCCCCCCCGCAGCCATGGAAACGGGGAAAGAGAACGGAGCCCGC AGAGGGACAAAAAGCCCGGAGCGGAAAAGGCGAAGCCCAGTCCAGCGGGTACTGTGCGAG AAGCTGAGGCCGGCCCAGGCCATGGATCCGGCTGGGGCCGAGGTCCCGGGCGAGGCC TTCCTGGCCCGGCGGCCGGATGGCGGCGGCGGGGATGTTCCTGCACGGCCGCGCTAC AGCCTCTTGGCGGAGATCGGGCGCGGCAGCTACGGCGTGGTTTATGAGGCTGTGGCTGGG CGCAGTGGGGCCAGGGTGGCAGTCAAGAAGATCCGCTGCGACGCTCCCGAGAACGTGGAG TTGGCACTAGCAGAATTCTGGGCCCTCACCAGTCTCAAGCGGCGCACCAGAATATCGTG CAGTTTGAGGAGTGCGTCCTACAGCGCAACGGGTTAGCCCAGCGCATGAGTCACGGCAAC AAGAACTCACAGCTTTACCTGCGCCTGGTGGAGACCTCGCTCAAAGGAGAAAGGATCCTG GGCTATGCTGAGGAGCCCTGCTATCTCTGGTTTGTCATGGAGTACTGTGAAGGTGGAGAC CTCAATCAGTATGTCCTGTCCCGGAGACCTGACCCAGCCAACAAAAGTTTCATGCTA CAGCTTACAAGCGCCATTGCCTTCCTGCATAAAAACCACATCGTGCACAGGGACCTAAAG CCAGACAACATCCTGATCACAGAGCGGTCTGGCACCCCCATCCTCAAGGTGGCAGACTTT GGACTGAGCAAGGTCTGTGCAGGGCTGGCACCCCGAGGCAAAGAGGGCAATCAAGATAAC AAAAATGTGAATGTGAATAAATACTGGCTGTCCTCAGCTTGTGGCTCAGACTTCTACATG GCTCCCGAAGTCTGGGAGGGACACTATACAGCCAAGGCGGACATCTTTGCTCTGGGCATT ATCATCTGGGCAATGATAGAAAGAATTACCTTTATTGACTCTGAAACCAAGAAGGAGCTC CTGGGGACCTACATTAAGCAAGGGACTGAGATCGTCCCTGTTGGTGAGGCGCTGCTAGAA AACCCAAAGATGGAGTTGCATATCCCCCAGAAACGTAGGACTTCCATGTCTGAGGGGGTC

#### FIGURE 2XXX

SEQ ID NO: 99 AA215311 H CGRCCGCGCTACGGAAAGCCGGAGGGGGGGGGGGGCCGTCGGCGTAAGGGGGTGTCCCGC GCGCACCACGGGGCGCGCCGGCTGCTGACTGGAGGCGGCGGCGGAGCGCGAGC TGCCCGATAATGGCGGCCTGCAGAGCCCATGAGAGGGAGAAGCGGCAGCGTCTACCCTGA GAAACCTCGACCTTGAAGATGGTGAGTAGCCAGCCAAAGTACGATCTAATACGGGAGGTA GGCCGAGGTAGTTACGGTGTTGTGTATGAAGCAGTCATCAGAAAGACCTCTGCACGGGTG GCAGTGAAGAAATTCGATGTCACGCACCTGAAAATGTTGAACTAGCCCTTCGTGAGTTC TGGGCACTAAGCAGTATCAAGAGCCAACATCCAAATGTGATTCACTTGGAGGAATGCATC CAGCTTGTAGAAACTTCATTAAAAGGAGAAATTGCCTTTGATCCCAGAAGCGCCTATTAT AAGCCCAATCGTAAAACTAACACCAGCTTCATGCTTCAGCTGAGCAGTGCCCTGGCTTTC TTGCATAAAAACCAGATCATCCACCGAGATCTTAAGCCTGATAACATCCTGATTTCTCAA ACCAGGTTGGATACCAGTGACTTGGAACCTACCCTCAAAGTGGCTGATTTTGGTCTAAGT AAAGTTTGTTCAGCCTCTGGGCAGAACCCAGAAGAACCTGTCAGTGTAAACAAGTGTTTC CTTTCCACAGCATGTGGAACAGATTTTTACATGGCTCCTGAAGTTTGGGAAGGACATTAC ACAGCAAAAGCTGACATCTTTGCTCTGGGGATTATCATCTGGGCAATGCTGGAAAGGATC ACATTCATAGACACAGAGACAAAGAAGGAACTCTTGGGGAGTTATGTAAAACAAGGAACT GAGATTGTGCCTGTTGGGGAGGCACTTCTGGAAAATCCCAAAATGGAACTTCTCATTCCT AACCCTCAGGATCGTCCAGATGCTTTTGAACTAGAACTCAGATTAGTACAAATTGCATTT AAAGATAGCAGCTGGGAAACGTGACACATATTATTTGCAAATACCATGGATGATATGCTG CTTCTGTTTAACAGTGATGCAACATTATGTGGCTGAAAAAGAATATAAAAAGCTAGACTC AAGTTGGCCGTTTTATTAGTATGTTTCAAATGTGTATTACCAATGTGGGTGTAAATTTTT AAAAAATGATTATTGATAGAAGTTTGGCAGGAAAATTCTTTAAGAGCTAACAAGAGAAGA GAGTCCAGTTTTCTGGAAATATGTCTTTAAGTATTTTAGACATTCCTCGTCAGTATTAGG AATTTCCATGGGAAAAGAGGTTTGCATGCTGGTAATGCAACCTTTGAAACTTTGTAAAGG AAACATATATGTATATTTATGTATATGTAAGTATGTGAATGTGCGCATTTTGCATTCC ATATGAAAAAATGCCACGTCTGTTTAAATTATTTGATGTAGGTTTTGGGTTTTTGAGATT TGCTGGTGAAGTCAGTGACGAAAAATAAACCTTCCCTTATCTTCCTACTCTGCCCCTCCC

CCTAATGAAATCATATTAAGTNGTTTTTCCTNNTTTTTTGTAATATACAGCTTTTTTTT TAAGGCATCATTTTCGAGGGTCTAAAATTATCTGGTAAAACAAATGAAATTAAGTGATCC AAAGCTGCTGAAGTATGTTTGAACTCTCCAGTGCCCTATAGCTGCAAGAGTTGAATTAGT

CATGCAGTCATATGGCAGCAGGTTGGTGATT

#### **FIGURE 2YYY**

GGTAGCCATAAAGTGTGTAGCCAAGAAAAGTCTGAACAAGGCATCGGTGGAGAACCTCCT CACGGAGATTGAGATCCTCAAGGGCATTCGACATCCCCACATTGTGCAGCTGAAAGACTT TCAGTGGGACAGTGACAATATCTACCTCATCATGGAGTTTTGCGCAGGGGGGCGACCTGTC TCGCTTCATCCATACCCGCAGGATTCTGCCTGAGAAGGTGGCGCGTGTCTTCATGCAGCA ATTAGCTAGCGCCCTGCAATTCCTGCATGAACGGAATATCTCTCACCTGGATCTGAAGCC ACAGAACATTCTACTGAGCTCCTTGGAGAAGCCCCACCTAAAACTGGCAGACTTTGGTTT CGCACAACACATGTCCCCGTGGGATGAGAAGCACGTGCTCCGTGGCTCCCCCCTCTACAT GGCCCCGAGATGGTGTGCCAGCGGCAGTATGACGCCCGCGTGGACCTCTGGTCCATGGG GGTCATCCTGTATGAAGCCCTCTTCGGGCAGCCCCCCTTTGCCTCCAGGTCGTTCTCGGA GCTGGAAGAGAAGATCCGTAGCAACCGGGTCATCGAGCTCCCCTTGCGGCCCCTGCTCTC CCGAGACTGCCGGGACCTACTGCAGCGGCTCCTGGAGCGGGACCCCAGCCGTCGCATCTC CTTCCAGGACTTCTTTGCGCACCCCTGGGTGGACCTGGAGCACATGCCCAGTGGGGAGAG AGCAGCCGCCTTATCACTCTACTGCAAGGCTCTGGACTTCTTTGTACCTGCCCTGCACTA TGAAGTGGATGCCCAGCGGAAGGAGGCAATTAAGGCAAAGGTGGGGCAGTACGTGTCCCG GGCTGAGGAGCTCAAGGCCATCGTCTCCTCTTCCAATCAGGCCCTGCTGAGGCAGGGGAC CTCTGCCCGAGACCTGCTCAGAGAGATGGCCCGGGACAAGCCACGCCTCCTAGCTGCCCT GGAAGTGGCTTCAGCTGCCATGGCCAAGGAGGAGCCGCCGGCGGGGAGCAGGATGCCCT GGACCTGTACCAGCACAGCCTGGGGGAGCTACTGCTGTTGCTGCGGAGCCCCCGGGCCGG AGGCGGGAGCTGCTTCACACTGAGGTTCAGAACCTCATGGCCCGAGCTGAATACTTGAAG GAGCAGATGAGGGAATCTCGCTGGGAAGCTGACACCCTGGACAAAGAGGGACTGTCGGAA TCTGTTCGTAGCTCTTGCACCCTTCAGTGACCCTAGAAGAATGATTGGACAGATGTGAGC CATCTGGAGCAGAGGGCACTAACCCAGGCTGACGCCAAGAATGAAGTGGCCCACTGCAG CCCTGGCGAGCAGCTTCTTGGATGGACAGTGCTGAGACCCCCATATCCCAGAGTCCCCA GCCTCCCTCAGGTTACTCTGCACCCCACAGATGGTTTGATGGCTGTGCTGTATACTGGAG GGGAGGGCAGGACTCTGGGAGAACAGCACTTCTTTCATGAGACCTTTGTTACTCGGTGGT TACTGGGTCCTGTGCCTGTTCGTTTTGGGGCATGCAGCCCTCTATCATTTTTTGGCTCCGA GAAGAGGGCAAGGGCCCCCGCAGGGTACTTCTGTGCTTGCCCTCGCCCTGCCAGCAGGC AGCTGTGCCCTGGCCTTCCCGGGACCCCTTATTCCAACTCAGCTCCTCTTTGCA CTGGAATGGGGCACTCCAACACCCCTCAGGGACCACCCTCCCCACAGTATGCACTCAGCC CCACAGAACCCACCAGTCTTTCTGGGAACTCACACCTGCCCGCCATCTTGGTACTTTAGG TTAATCCCTCAAGCATGAAAGCTGGATCTTTTGGGGTTTAAGAAGCCCAAGCCTTGTTCC TGCCCTGGCCTAGGGAGCACTCAGGAGGGTTCCTTGGTCCTCATCTCTCCCACCTCCGTT CCCTCTGGGCCCCACACTAGCCACAGCGGGGCCTTGTGCTGGAGTTTGAGCCTGGGACA CTGCCCTGCCGCCGTGGAGCCCTGGGCAAGCTCTTTCCCCTTTCTGGGCCTGGGTCTCCC CATCTCTTCAATGGGGCTGATACCTTCACAGCCCACAGCATGGGCACTTATGAGGACAAA GTGAATTTAACCTGGAAAAGAATGTATTTGAGAGTTTCTTTTAAATAATCAGCGGGTGTT TGCAGGAGGCTGAGTGTGAAGAGTATCATTCATTGTTTCTCTATTAAATTATTTTCTCT

SEQ ID NO: 101\_AA311714\_H
TGGACCTGTCCTGAGGCAGAGGCCGAGATGCGCGCAACCGCGGGAGCAGCCAAGTGGACT
GGACTCTTTTCTTGACTTAGCTACCAGGAGCTAGAGATGCTGTTATTCTATCGTATGTGA
GAAGTCGGCCCAGAGATGGAAAACTTTATTCTGTATGAGGAGATCGGAAGAGGAAGCAAG
ACTGTTGTCTATAAAGGGCGACGGAAGGGAACAATCAATTTTGTAGCCATTCTTTGTACT
GATAAGTGCAGAAGGCCTGAAATAACCAACTGGGTCCGTCTCACCCGTGAAATAAAACAC
AAGAATATTGTAACTTTTCATGAATGGTATGAAACAAGCAACCACCTCTGGCTAGTGXAT
GAAAACCTCCCAGAAGATGTTGTGAGAGAATTTGGAATTGACCTGATTAGTGGATTACAT
CATCTTCATAAACTTGGCATTCTCTTTTTGTGACATTTCCCTAGGAAGATACTCTTTGGAA

#### FIGURE 2ZZZ

GGGCCTGGCACACTGAAGTTTAGCAACTTTTGCTTGGCAAAAGTGGAAGGTGAAAATTTG GAAGAGTTCTTTGCTTTGGTGGCAGCAGAGGAGGAGGAGGTGATAATGGGGAAAATGTC CTGAAGAAAAGCATGAAAAGTAGAGTCAAAGGATCTCCTGTATATACAGCACCAGAAGTT GTGAGGGGTGCTGACTTTTCCATCTCCAGTGACCTCTGGTCTTTGGGCCTGTCTGCTTTAT GAAATGTTTTCAGGAAAACCTCCATTCTTCTCAGAAAGTGTTTCAGAATTAACTGAAAAG ATCTTATGTGAAGATCCTTTGCCACCTATTCCGAAAGATTCTTCTCGTCCTAAAGCTTCT TCAGATTTTATTAATTTGCTTGATGGGTTACTTCAAAGAGATCCTCAGAAAAGATTGACT TGGACAAGGCTACTGCAGCATTCATTTTGGAAGAAAGCTTTTGCTGGAGCAGATCAGGAA TCAAGCGTCGAAGATCTCAGTCTCAGCAGAAACACTATGGAGTGTTCTGGGCCACAAGAT TCCAAGGAGCTTTTGCAGAACTCTCAGAGTAGACAAGCAAAAGGGCACAAGAGTGGTCAA CCACTAGGTCACTCTTCAGACTAGAAAATCCAACTGAGTTTCGGCCTAAGAGTACTCTT GAGGGTCAATTGAATGAATCCATGTTTCTTCTCAGTTCTCGTCCTACTCCCAGAACTAGC ACTGCAGTGGAAGTAAGTCCTGGTGAGGATATGACTCACTGTTCACCACAGAAGACTTCT CCTCTGACCAAGATTACAAGTGGACACCTGAGTCAGCAGGACCTGGAATCCCAGATGAGA GAGCTTATCTACACGGACTCAGATCTTGTTGTCACCCCCATTATCGACAATCCAAAGATA ATGAAACAGCCACCAGTTAAATTTGATGCAAAAATATTGCATCTACCAACATATTCAGTG GATAAGTTATTTCTGAAAGATCAAGATTGGAATGACTTTTTGCAACAAGTGTGCTCG CAGATCGACTCCACTGAGAAGAGCATGGGGGCCTCCCGAGCCAAGCTGAATCTCCTTTGC TATTTGTGCGTGGTCGCCACCAGGAGGTGGCCACCAGGCTCCTCCATTCCCCCCTG TTCCAATTGCTAATCCAGCATTTGCGGATAGCTCCAAACTGGGATATACGGGCCAAGGTT GCTCACGTGATTGGTTTACTGGCTTCGCACACACTGAGCTCCAGGAAAATACACCTGTT GTTGAGACTACAAGCTCCATTGGAATCGGGATTTTGAACTGTCTTGTTCAACACTCCACT AAACTGTATCAGCATT

SEQ ID NO: 102\_SGK384\_H
TCTTTGGCCCACGTGCTGAGGGCCGGCAGATCCTGACGGAGCCAGAAGTGCGCGACTAC
CTGCGGGGCCTGGTCAGCGGCCTGCGCTACCTGCACCAGCGGTGCATCCTGCACCGC

SEQ ID NO: 103 AA210451 M SGK384 M GGTCTGCTGCATGGATAATGGACTGGAACACAGAAAGACCATGCAGGGTTCGGCTGTAGA AGGCCAGTATCTCCAGAGGCCAGAAGACACCATCAGATCTCCTGGGACTGGAGTTATAGA AACCCTGCTGGGAGAAAAAAGAAACTGCTGAAGGGACTGACATGGGACAGCAACATGGAA CCAGGAATGGTCTCACGCATAGAGAGCTCCCCCGGGGCGTGGGGCTGCTGCTCGCCATGG CCCTTATGAACGTGGCGCTCTACCTCTGCCTTGATCAGCTTTTCATCTCCCCTGGACGAT CCACCGCGGACTCTAGGCGCTGTCCTCCGGGCTACTTCAGAATGGGGCGGATGAGAAACT GCTCACGCTGGCTGTCCTGTGAAGAGCTGAGGACAGAAGTCAGGCAGCTGAAGCGCGTTG CCCGGCTCACCAGGCTGGAGATGAAGGAGGACTTCCTGCATGGGCTGCAGATGCTGAAGT CTCTACAGAGTGAGCACGTGGTCACGCTGGTGGGCTACTGTGAGGAAGATGGCACTATTC TCACCGAATATCACCCCTTAGGTTCCTTGAGCAACCTGGAAGAAACACTAAACCTTTCAA AGTACCAAGACGTGAACACTTGGCAGCACAGGCTGCAGCTGGCCATGGAGTACGTCAGCA TCATTAACTATCTGCATCACAGCCCCCTGGGCACGAGGGTCATGTGTGACTCTAACGACC TGCCCAAAACATTGTCCCAGTACCTGCTAACAAGTAACTTCAGCATTGTGGCAAACGACC TGGACGCTCTGCCCCTGGTAGACCATGACTCTGGGGTACTTATAAAGTGTGGCCACAGAG AGCTCCATGGGGATTTTGTGGCTCCAGAGCAGCTGTGGCCCTACGGAGAAGACACGCCCT TCCAAGACGATCTCATGCCTTCCTACAATGAGAAGGTTGACATCTGGAAGATTCCAGATG ATATCCATAAGGCGTGCAAGAGCCAGATCCCGGCAGAAGACCCACTGCTCAGAACGTGC

PCT/US00/14842

#### **FIGURE 2AAAA**

TAGACGCTTACCAGAGGGTTTTCCATTCACTCCGAGACACTGTGATGTCGCAGACGAAAG AAATGCTGTAAAAATGAGCCATCGAGTGACGTGCTTGATGGCTGAATGGCATCCCAGCTG ACGTAGGCCTCCTCTACGTCTGCCTGCATGTTTGAGTGTTCTGCTCTCCTGGCAGCCCGG ATGGAAGCTGCCAAGCGAGAAAGCCTGGCTTCAGGATGCTCCCTGGTGAAGATGCAGAGG ATTCTGGATCTGCATAGTTTCAAGGGAGTGATCAAACGGTGACCTTGAAGACATGCTGCC TGCCTTGGTAACTTTTTATAGACTAGTAGGAAACAGAAATCTTTTGGGGGAGGGGGGGAC AACCCACTAGTTCCTCAGAGACAATTTCTTCTCATTCAGAAAGCCCTGTTGGAAGCTGGG GATGTTTTAACTCCGTGGCAGGGCACTTGCCTAGTTGTGTGCAAAGCCTTGGATCTGACC CATGGCATGTGCACACACACAAATGCTCAAAGAAAATCCCAGACGCCAGAAGTGTGCCCC  ${\tt CTGACTCGTGTCACTGAGCCAAGTGTGCATGGTCGTTAGCTACTTTGTGGGTTCTTCTTT}$ AAGGAAAGTGGGCACTGTTATATTGTTGGACGACTTCTTGCTGATTAAGGGGTGTCGAGT CACGACCACTTCACAAACACCGACCAACAGCAAACAACCACCCCGCTTCTCGGGGG CCCTAGCACTTATGTACTTCTGAAAAGTCCCCAGAAATTCCAATCATCACACACTCAGAG AAACTGTCTGCTGCCAAAACTACACCCCTGCTAGAGCATGAGGCAAATCATAGTCAG CTGCTGTGGACAGTCTGAAGCAGCCTGGCATCCCACACCTGAGATTAAAACAAAAACATT CTTACCTGTGTTTTTGTTTTTAAGAAACCAAAGTGCACCAAGATAGCATGCTCTTG AGATTGTGGCTGTCTAGAGATTTTTGGAACAGCAAGTTGAAGGAACTTTCTTACCTGCCT TGAATGGTGCTTTGAACTTCCTGCTGACCTGGAGTTTCTGTGTGAATATTTCTATCCAGT GTCCCCCTGTACCGGAAAGTACAAAGTCTGCTCTGGGCTTGCATGCCTGAACACTTTAAA ACACTGTGGAGCCAGGAATAATGGTACCCACCTGTAATCCCAGCACCTGGGAGACAGGAG GAACCAGGAGTTCAGGGTTATCCTGGGCTATATACCGTGACCCTGTCTACCCCCACACCC CAATAAAAAAACAAAAAGGTC

SEQ ID NO: 104 SGK071 2 H GAGGTGGTGGCTGTGCAGATGATGGTGGAATGCATGATGACCATTACGCCAGTCAGGCC CTGGAGGAGCTGATGCCACTGCTGAAGCTGCGGCACGCCCACATCTCTGTGTACCAGGAG CTGTTCATCACGTGGAATGGGGAGATCTCTTCTCTGTACCTCTGCCTGGTGATGGAGTTC AATGAGCTCAGCTTCCAGGAGGTCATTGAGGATAAGAGGAAGGCAAAGAAAATCATTGAC TCTGAGTGGATGCAGAATGTGCTGGGCCAGGTGCTGGACGCGCTGGAATACCTGCACCAT TTGGACATCACAGGAATCTCAAACCCTCCAACATCATCCTCAFCAGCAGTGACCAC CGTGCGGAGGAAGACCCCTTTCGTAAGTCCTGGATGGCCCCTGAAGCCCTCAACTTCTCC TTCAGCCAGAAATCAGACATCTGGTCCCTGGGCTGCATCATTCTGGACATGACCAGCTGC TCCTTCATGGATGGCACAGAAGCCATGCATCTGCGGAAGTCCCTCCGCCAGAGCCCAGGC AGCCTGAAGGCCGTCCTGAAGACAATGGAGGAGAAGCAGATCCCGGATGTGGAAACCTTC AGGAATCTTCTGCCCTTGATGCTCCAGATCGACCCCTCGGATCGAATAACGATAAAGGAC GTGGTGCACATCACCTTCTTGAGAGGCTCCTTCAAGTCCTCGTGCGTCTCTCTGACCCTG CACCGGCAGATGGTGCCTGCGTCCATCACCGACATGCTGTTAGAAGGCAACGTGGCCAGC ATTTTAGGTGATGCTGGGGACACAAAGGGGGGAGCGTGCCCTGAAGCTCCTGTCCATGGCC ATGCACGACCAGTGGCTCAGCTGTGACCAGGACAGAGTCCCTGGGAAGAGAGACTTTGCC TCCTGGGGAAACTAGGGAAGCTGTTGGGCCCCATCCCAAAGGGTCTGCCGTGGCCCCCG GAGCTGGTGGAGGTGGTCACGACCATGGAGCTACATGACAGGGTCCTCGATGTCCAG CTGTGTGCCTGCTGCTGCTGCACCTCCTGGGCCAAGCGCTGGTGCACCACCCGGAA GCCAAGGCTCCCTGCAACCAAGCCATCACCTCCACCCTGCTGAGTGCTCTTCAGAGCCAC CCCGAGGAGGAGCCACTTCTTGTCATGGTCTACAGCCTGCTAGCCATCACCACAACCCAG

#### **FIGURE 2BBBB**

SEQ ID NO: 105 AA118352 M SGK071 M CAGAAGAAGACCCCTGCCAGAAGTCCTGGATGGCTCCTGAAGCTCTCAAATTCTCCTTCT CCACCAAATCCGACATCTGGTCTCTGGGCTGCATCATTCTAGACATGGCCACTTGCTCCT TCCTGAACGACACAGAAGCCATGCAACTGCGGAAGGCCATCCGCCATCATCCAGGCAGCC TGAAGCCCATCCTGAAAACCATGGAGGAGGAAGCAAATCCCTGGTACAGATGTCTACTATT TGCTTCTGCCCTTCATGTTGCATATCAACCCCTCCGATCGACTGGCAATCAAGGATGTGA TGCAAGTCACCTTCATGAGCAACTCCTTCAAAAGCTCCTCTGTTGCGCTGAATATGCAGC GGCAGAAGGTCCCCATCTTCATCACTGACGTGCTGCTTGAAGGCAACATGGCCAACATCT TAGGCAGCTGGCTGTGTCCTTTGTGAACGACAGCAGCACTGTGACTCAGGGATTG GCTCGCAGAGACTTGGGTTTGATTTTCAGTCAGTCTCTTGGACAGAGCACCCTCTGAAAG ATGTCATGCAGAATTTCTCCAGTCGACCAGAGGTCCAGCTCAGAGCCATTAACAAGTTGT TGACAATGCCAGAGGACCAGCTAGGGCTGCCATGGCCCACAGAGCTGCTGGAAGAGGTGA TCAGCATCATAAAGCAGCATGGGCGGATCCTGGATATTCTGCTCAGCACCTGCTCCCTTC TGCTGCGTGTTCTTGGCCAAGCACTGGCAAAGGACCCAGAAGCTGAGATCCCAAGGAGCA GTTTGATCATCTCCTTGCTGATGGATACCTTGCGGAGCCATCCTAACTCTGAAAGGCTTG TTAATGTGGTCTACAACGTGCTTGCCATTATTTCCAGCCAAGGACAGATCTCAGAAGAGC TGGAAGAGGGGGTTGTTTCAGCTTGCCCAAGAGAACCTGGAGCACTTCCAAGAGGACA GGGACATCTGCCTCTATCCTGAGCCTGCTCTGGTCCCTCCTGGTAGATGTTGTCACTG TGGACAAGAGCCCTTGGAGCAGCTCTCTGGCATGGTCACCTGGGTGCTGGCTACTCATC CGGAGGACGTGGAAATAGCAGAGGCTGCTGTGCGGTGCTCTGGCTGTCCTTGTTGG GCTGCATAAAGGAGAGTCAGTTTGAGCAGGTGGTAGTGCTCCTGAGAAGCATCCAGC TGTGCCCTGGCAGAGTACTGCTGGTGAACAATGCATTCCGTGGCTTGGCCAGCCTCGCAA AGGTGTCCGAACTGGTGGCCTTCCGAATAGTAGTACTGGAAGAGGGCAGCAGCGGCCTCC ACCTCATCCAAGATATCTACAAGCTCTACAAGGATGACCCTGAGGTGGTGGAGAACCTCT GCATGCTGTTGGCCCATCTGACCTCCTACAAGGAGATCCTGCCAGAGATGGAGTCTGGAG GCATCAAAGACCTAGTCCAGGTGATCCGGGGGCGCTTTACCTCCAGCCTGGAGCTGATTT CTTACGCTGATGAGATACTCCAGGTACTGGAAGCAAATGCACAACCTGGCCTCCAGGAGG ATCAGCTTGAGCCTCCTGCAGGGCAGGAAGCCCCACTGCAGGGAGAGCCCCTCTTCAGGC CCTGACATGCTGCCCTTCTGGTCCTGTGGTAAGAGAAAGTATCACTAGGTCCAGTATTAA TTTCGTACCCCATGGTGACTAATAAAAGAAGCCCTAGGCTGTTTCTGGC

#### FIGURE 2CCCC

CGCCTCCTTCCTGCTGGGCTCCGTCCTCAACGTGCTCTTCGCTCCGGGTCGGAGCCTCCG AGGCCAGGCCAGTCCCCTGAGCCTTCGCCGGCCCCGGGTGCGGGCCGTCGCGGGGCCGC GGGGAGCTGGCCCGGCAGATCCGGGCGCGCTACGAGGAGGTGCAGCGCTATTCCCGCGGG GGCCCCGGGCCCGGGCCGGCCGGAGCGCCGCCCTGATGGACCTGGCTCCGGGC GGGCCCGGCCTGCCGCCCCCGGCCCCCTTGGGCCCCGGCCCCTGTCCGACGGCGCCCCA GCGCTTCGCAACGTGTCCGGCGCGCAGTACATGGGCTCAGGCTACACCAAGGCCGTGTAC CGGGTCCGCCTGCCCGCGGTGCCGCGGTGGCGCTCAAGGCGGTGGACTTTAGCGGCCAC GATCTGGGCAGCTGCGTGCGCGAGTTCGGGGTACGGAGGGGCTGCTATCGGCTGGCGGCC CACAAGCTGCTTAAGGAGATGGTGCTGCTGGAGCGGCTGCGGCACCCCAACGTGCTGCAG CTCTATGGCTACTGCTACCAGGACAGCGAGGACATCCCAGACACCCTGACCACCATCACG GAGCTGGGCGCCCTGTAGAAATGATCCAGCTGCTGCAAACTTCCTGGGAGGATCGATTC CGAATCTGCCTGAGCCTGGGCCGCCTCCTCCACCACCTGGCCCACTCCCCACTGGGCTCC GTCACTCTGCTGGACTTCCGCCCTCGGCAGTTTGTGCTGGTGGATGGGGAGCTCAAAGTG CTCGAGTTTCCGGCCAGGAACTTCACCCTGCCCTGCTCAGCCCAGGGCTGGTGCGAGGGC ATGAACGAGAAGCGGAACCTCTATAATGCCTACAGGTTTTTCTTCACATACCTCCTGCCT CACAGTGCCCCGCCTTCACTGCGTCCTCTGCTGGACAGCATCGTCAACGCCACAGGAGAG CTCGCCTGGGGGGTGGACGAGACCCTGGCCCAGCTGGAGAAGGTGCTGCACCTGTACCGG AGCGGGCAGTATCTGCAGAACTCCACGGCAAGCAGCAGTACCGAGTACCAGTGTATCCCA GACAGCACCATCCCCCAGGAAGACTACCGCTGCTGGCCATCCTACCACCACGGGAGCTGC CTCCTTTCAGTGTTCAACCTGGCTGAGGCTGTGGATGTCTGTGAGAGCCATGCCCAGTGT CGGGCCTTTGTGGTCACCAACCAGACCACCTGGACAGGTCGGCAGCTGGTCTTTTTCAAG ACTGGATGGAGCCAAGTGGTCCCTGATCCCAACAAGACCACATATGTGAAGGCCTCTGGC TGACCTATCTGAGGGCTCGGCTGACCAGCTGACTATCCTCAGCAGCTGGGCTTGCCTGTG GAGGGAGTGACTTGCACTGGCAGCACTGCATGTCACCTGGGAACCCCTGCAGACAAAGCT AACATCCCAGACAGACAGATGTGACCAGGACAAACGTGCAATAATGCCAAATGTTAAAAT GTGAGTTTACCAGCCTAGCTATGGGACTGCTGGCTCCTAGTCCAGGAATCATGGGGGTAT GACTGCCTCTCCAACCCTGTGGGCTGTAAGCAAGCTCAGGCTAGTCTCCCCACTGGGGGC TGTGCCCCTCCCTGGGACGGTTCCGTGGGCAGCCCCATCACTGTGTTCAATAGTGTGAGA ATGTAGCTAAAGCCCCTGCTGCTGCTGCACATGCCACAGCAGGCGGTGGGGGCTGCG TGGGGACAATCCATCGTGGAGTGTTCTCTCAGCTTAGGTCTGGACAGGAGACTTGGCGGG AGATGCTCCAGGATGTGGGTGATTCTGTACCTGGGGAGGCTATCTCTGACCTCCCGACAG -GGGACACTCCCAGGCCAGGCCAGGGGTCAGGGGCAGAGGTGCACACCTCAGCATGAGCCA AGACTGGGGTCAGGGAGCAGGTGTGGTTTGAGCCAGGACCTGGGGCGGGGGTGGGGCCGG GGCCTTTCTGCCTCATTTGCTTTCAATGAAAGCCTCAAAGCAGCCAAAACCAGGCTTTCC CCCTTCCTCGAGTTTGAATATCCAGAATCTTTTGTACTTCTTGTTGGTTAAATTGTTTAT TTTTGTAAAAATAAAATAAAATTAGTTAATAAAATGATGTTTCACAGCAAACTCTTCCC

#### FIGURE 2DDDD

CCAGCAGTGCCGACTGCACGCTAGAGTTTCCAGCCAGGAACTTCAGCCTGCCCTGCTCGG CCCAGGGCTGGTGCGAGGGCATGAATGAGAAACGGAACCTCTACAATGCCTACAGGTTCT TCTTCACATACCTCCTGCCACACAGTGCCCCGCCTTCCCTCCGACCTCTCCTGGATAGCA TCGTCAATGCCACGGGAGAGCTCGCCTGGGGGGGTGGATGAGACCCTGGCCCAGCTGGAGA CAGCGCTACACTTGTTCCGAAGTGGGCAGTACCTGCAGAACTCTACAAGCAGCAGGGCTG AGTACCAGCGCATCCCGGACAGTGCCATCACACAGGAGGACTATCGCTGCCGGCCATCCT ATCACCACGGCGGCTGCCTCTGTCCGTGTTCAACCTGGCTGAGGCTATAGATGTCTGTG AGCTGGTCTTTTTTAAGACTGGATGGAACCAAGTGGTCCCTGATGCCGGCAAGACCACAT ATGTGAAGGCCCCTGGTTGACTGGTTGTGGGCTCAGCTGACCAGCTGGGCTTGCCTG CTGATGTGACCAGGACAAAACGTGCAATATGCAAAAATGTTAAAATGTGAGTTTGCCAGC TTCAGTCCCAGACTGGTTGGAACCCGATTGCCTCTCTGGAGCTGTAGGCTGTGAGCAGGG CTCAGGCTGGTCTTAACTGGGACAGTCCCGTGGGCAGCCCATTACTGCATTCATGCTTTG AGAATGTAGCCAGAACACTGCTGCTGCATAAGCCACCGTGGGCAGGAGCTGCCTGGGGAC AACCAGTCTCAGAGTGCTCTCAGCTCAGCTCCGCTCCAAATGGAGAGCGCGGGATGCG GAGATGTGAGTGAACCAGCACTGGGAAGAAGGCTCTCGGGGCCTCTCCCTAGAGGTTGCTC CTAGGCCAGCCCGAGGCCGTGGGCAGCAGTGCTCGCATCCATATGAGCCAAGACTAGAG TGGAGGAGCAGATTGCATTTGAGCCAGGACTGGGGTGGGGGTAGGGTCGGGGCCTCTCTG CCTCATTTGCTTTCAGTGAAAGCCAGGGAGCCAGCCAGGCCAGCCCACTCCTGG AGGCCAGGCTCCTCCCCCTCCTGGAGGCCAGGCTCCCCCCCTCCTGGAGTTTGCGTACC CAATTAATAAAATGATGTTTTGTGAC

SEQ ID NO: 108 VRK3 H

ATGATCTCCTTCTGTCCAGACTGTGGCAAAAGTATCCAAGCGGCATTCAAATTCTGCCCC TACTGTGGAAATTCTTTGCCTGTAGAGGAGCATGTAGGGTCCCAGACCTTTGTCAATCCA CATGTGTCATCCTTCCAAGGCTCAAAGAGAGGGCTGAACTCCAGTTTTGAAACCTCTCCT AAGAAAGTGAAATGGTCCAGCACCGTCACCTCTCCCCGATTATCCCTCTTCTCAGATGGT GACAGTTCTGAGTCTGAAGATACTCTGAGTTCCTCTGAGAGATCCAAAGGCTCCGGGAGC  ${f AGACCCCAACCCCAAAAGCAGCCCTCAGAAGACCAGGAAGAGCCCTCAGGTGACCAGG}$ GGTAGCCCTCAGAAGACCAGCTGTAGCCCTCAGAAGACCAGGCAGAGCCCTCAGACGCTG AAGCGGAGCCGAGTGACCACCTCACTTGAAGCTTTTGCCCACAGGGACAGTGCTGACAGAC AAGAGTGGGCGACAGTGGAAGCTGAAGTCCTTCCAGACCAGGGACAACCAGGGCATTCTC TATGAAGCTGCACCCACCTCACCTGTGACTCAGGACCACAGAAGCAAAAGTTC TCACTCAAACTGGATGCCAAGGATGGGCGCTTGTTCAATGAGCAGAACTTCTTCCAGCGG GCCGCCAAGCCTCTGCAAGTCAACAAGTGGAAGAAGCTGTACTCGACCCCACTGCTGGCC ATCCCTACCTGCATGGGTTTCGGTGTTCACCAGGACAAATACAGGTTCTTGGTGTTACCC AGCCTGGGGAGGAGCCTTCAGTCGGCCCTGGATGTCAGCCCAAAGCATGTGCTGTCAGAG AGGTCTGTGCTGCAGGTGGCCTGCCGGCTGCTGGATGCCCTGGAGTTCCTCCATGAGAAT GAGTATGTTCATGGAAATGTGACAGCTGAAAATATCTTTGTGGATCCAGAGGACCAGAGT CAGGTGACTTTGGCAGGCTATGGCTTCGCCTTCCGCTATTGCCCAAGTGGCAAACACGTG GCCTACGTGGAAGGCAGCAGGAGCCCTCACGAGGGGGGACCTTGAGTTCATTAGCATGGAC CTGCACAAGGGATGCGGGCCCTCCCGCCGCAGCGACCTCCAGAGCCTGGGCTACTGCATG CTGAAGTGGCTCTACGGGTTTCTGCCATGGACAAATTGCCTTCCCAACACTGAGGACATC ATGAAGCAAAAACAGAAGTTTGTTGATAAGCCGGGGCCCTTCGTGGGACCCTGCGGTCAC TGGATCAGGCCCTCAGAGACCCTGCAGAAGTACCTGAAGGTGGTGATGGCCCTCACGTAT GAGGAGAAGCCGCCCTACGCCATGCTGAGGAACAACCTAGAAGCTTTGCTGCAGGATCTG CGTGTGTCTCCATATGACCCCATTGGCCTCCCGATGGTGCCCTAG

#### **FIGURE 2EEEE**

SEQ ID NO: 109 S71575 M VRK3 M CCATCCCCACCTGTATCGGCTTTGGCATTCACCAGGACAAGTACAGGTTCCTAGTATTCC CCAGCCTGGGGAGGAGCCTTCAGTCAGCCCTGGATGACAACCCAAAGCATGTGGTATCAG AGAGATGTGTGCTTCAGGTGGCCTGCAGGCTGCTGGATGCTCTGGAGTATCTCCATGAAA ATGAGTATGTTCACGGGAACCTGACAGCTGAGAATGTCTTTGTGAATCCAGAGGATCTGA GCCAGGTGACCCTGGTGGGCTATGGCTTCACCTACCGATACTGCCCAGGTGGCAAACACG TGGCCTACAAGAAGGCAGCAGGAGTCCACACGATGGGGACTTGGAGTTCATTAGCATGG ACCTGCACAAGGGATGCGGACCCTCCCGCCGCAGCGATCTCCAGACCTTGGGCTACTGTA TGCTCAAGTGGCTTTATGGGTCCCTGCCATGGACAAATTGCCTTCCCAACACCGAAAAGA TAACTAGGCAGAAGCAGAAGTATCTGGACAGCCCCGAGCGCCTCGTGGGACTGTGTGGCC GCTGGAACAAGGCCTCAGAGACCCTGCGGGGAGTACCTGAAGGTGGTGATGGCCCTCAATT ATGAGGAGAAGCCACCCTATGCCACGCTGAGGAACAGCCTAGAAGCTCTGCTGCAGGATA TGCGGGTGTCACCCTATGACCCTCTGGACCTCCAGATGGTGCCTTAGATGGAATCCAGAG CTTCCGACTTGCAGCTTGAAGTAGAACATGAAGTAGTGTGACTGGAGGCCTGTTTGAACT CATAGCTCCTAAAAGAATCCCTTGAATGTGCATTCTCACCGCTCCCTTAGGACATATGAA TCAGCACTTGTGTTGGGGAACCTGAGTCATGTCATGTAATGTGAAACTCCTCCCTGTCTC AGCTCTGGCAGCTGTGGATGGAGGTAAGTGGATGCTGGCGGCGGCGGCGGCAGCAGCCAC TCCACTCCCTATGGCATTTCTGTGATGGCATAATAAACTGTTTTTAATC

SEQ ID NO: 110 AA45427 H ATGGGCCACGCGCTGTGTCTCTCCTCGGGGAACTGTCATCATTGACAATAAGCGCTAC CTCTTCATCCAGAAACTGGGGGGGGGGGGTTCAGCTATGTGGACCTAGTGGAAGGGTTA CATGATGGACACTTCTACGCCCTGAAGCGAATCCTGTGTCACGAGCAGCAGGACCGGGAG GAGGCCCAGCGAGAAGCCGACATGCATCGCCTCTTCAATCACCCCAACATCCTTCGCCTC GTGGCTTACTGTCTGAGGGAACGGGGTGCTAAGCATGAGGCCTGGCTGCTGCTACCATTC TTCAAGAGAGGTACGCTGTGGAATGAGATAGAAAGGCTGAAGGACAAAGGCAACTTCCTG ACCGAGGATCAAATCCTTTGGCTGCTGCTGGGGATCTGCAGAGGCCCTTGAGGCCATTCAT GCCAAGGGTTATGCCCACAGAGACTTGAAGCCCACCAATATATTGCTTGGAGATGAGGGG CGCCAGGCTCTGACCCTGCAGGACTGGGCAGCCCAGCGGTGCACCATCTCCTACCGAGCC CCAGAGCTCTTCTCTGTGCAGAGTCACTGTGTCATCGATGAGCGGACTGATGTCTGGTCC CTAGGCTGCGTGCTATATGCCATGATGTTTGGGGAAGGCCCTTATGACATGGTGTTCCAA AAGGGTGACAGTGTGGCCCTTGCTGTGCAGAACCAACTCAGCATCCCACAAAGCCCCAGG CATTCTTCAGCATTGCGGCAGCTCCTGAACTCGATGATGACCGTGGACCCGCATCAGCGT CCTCACATTCCTCCTCCTCAGTCAGCTGGAGGCGCTGCAGCCCCCAGCTCCTGGCCAA CATACTACCCAAATCTGA

#### FIGURE 2FFFF

GGGGGCCCCTGCCTTCCCCTTGGCCATCAAGATGATGTGGAACATCTCGGCAGGTTCCTC CAGCGAAGCCATCTTGAACACAATGAGCCAGGAGCTGGTCCCAGCGAGCCGAGTGGCCTT GGCTGGGGAGTATGGAGCAGTCACTTACAGAAAATCCAAGAGGGGTCCCAAGCAACTAGC CCCTCACCCCAACATCATCCGGGGTTCTCCGCGCCCTTCACCTCTTCCGTGCCGCTGCTGCC AGGGCCCTGGTCGACTACCCTGATGTGCTGCCCTCACGCCTCCACCCTGAAGGCCTGGG CCATGGCCGGACGCTGTTCCTCGTTATGAAGAACTATCCCTGTACCCTGCGCCAGTACCT TTGTGTGAACACCCCAGCCCCGCCTCGCCGCCATGATGCTGCTGCAGCTGCTGGAAGG CGTGGACCATCTGGTTCAACAGGGCATCGCGCACAGAGACCTGAAATCCGACAACATCCT TGTGGAGCTGGACCCAGACGGCTGCCCCTGGCTGGTGATCGCAGATTTTGGCTGCCT GGCTGATGAGAGCATCGGCCTGCAGTTGCCCTTCAGCAGCTGGTACGTGGATCGGGGCGG AAACGGCTGTCTGATGGCCCCAGAGGTGTCCACGGCCCGTCCTGGCCCCAGGGCAGTGAT TGACTACAGCAAGGCTGATGCCTGGGCAGTGGGAGCCATCGCCTATGAAATCTTCGGGCT TGTCAATCCCTTCTACGGCCAGGGCAAGGCCCACCTTGAAAGCCGCAGCTACCAAGAGGC TCAGCTACCTGCACTGCCCGAGTCAGTGCCTCCAGACGTGAGACAGTTGGTGAGGGCACT GCTCCAGCGAGAGGCCAGCAAGAGACCATCTGCCCGAGTAGCCGCAAATGTGCTTCATCT AAGCCTCTGGGGTGAACATATTCTAGCCCTGAAGAATCTGAAGTTAGACAAGATGGTTGG CTGGCTCCTCCAACAATCGGCCGCCACTTTGTTGGCCAACAGGCTCACAGAGAAGTGTTG TGTGGAAACAAAATGAAGATGCTCTTTCTGGCTAACCTGGAGTGTGAAACGCTCTGCCA GGCAGCCCTCCTCCTCTCATGGAGGGCAGCCCTGTGATGTCCCTGCATGGAGCTGGT GAATTACTAAAAGAACATGGCATCCTCTGTGTCGTGATGGTCTGTGAATGGTGAGGGTGG GAGTCAGGAGACAAGACAGCGCAGAGAGGGCTGGTTAGCCGGAAAAGGCCTCGGGCTTGG CAAATGGAAGAACTTGAGTGAGAGTTCAGTCTGCAGTCCTCTGCTCACAGACATCTGAAA AGTGAATGGCCAAGCTGGTCTAGTAGATGAGGCTGGACTGAGGGGGGGTAGGCCTGCATC CACAGAGAGGATCCAGGCCAAGGCACTGGCTGTCAGTGGCAGAGTTTGGCTGTGACCTTT GCCCCTAACACGAGGAACTCGTTTGAAGGGGGCAGCGTAGCATGTCTGATTTGCCACCTG GATGAAGGCAGACATCAACATGGGTCAGCACGTTCAGTTACGGGAGTGGGAAATTACATG AGGCCTGGGCCTCTGCGTTCCCAAGCTGTGCGTTCTGGACCAGCTACTGAATTATTAATC TCACTTAGCGAAAGTGACGGATGAGCAGTAAGTAAGTGTGGGGGATTTAAACTTGAG GGTTTCCCTCCTGACTAGCCTCTCTTACAGGAATTGTGAAATATTAAATGCAAATTTACA ACTGCAGATGACGTATGTGCCTTGAACTGAATATTTGGCTTTAAGAATGATTCTTCTTAT ACTCTGAAGGTGAGAATATTTTGTGGGCAGGTATCAACATTGGGGAAGAGATTTCATGTC TAACTAACTAACTTATACATGATTTTTAGGAAGCTATTGCCTAAATCAGCGTCAACATG CAGTAAAGGTTGTCTTCAACTGACAAAA

## SEO ID NO: 112 AI086865 H

AATGAGATGGAGAAGTACGAGCGGATCCGAGTGGTGGGGAGAGGTGCCTTCGGGATTGTG
CACCTGTGCCTGCGAAAGGCTGACCAGAAGCTGGTGATCAAGCAGATTCCAGTGGAA
CAGATGACCAAGGAAGAGCGGCAGGCAGCCCAGAATGAGTGCCAGGTCCTCAAGCTGCTC
AACCACCCCAATGTCATTGAGTACTACGAGAACTTCCTGGAAGACAAAGCCCTTATGATC
GCCATGGAATATGCACCAGGCGGCACTCTGGCTGAGTTCATCCAAAAGCGCTGTAATTCC
CTGCTGGAGGAGGAGACCATCCTGCACTTCTTCGTGCAGATCCTGCTTGCACTGCATCAT
GTGCACACCCACCTCATCCTGCACCGAGACCTCAAGACCCAGAACATCCTGCTTGACAAA
CACCGCATGGTCGTCAAGATCGGTGATTTCGGCATCTCCAAGATCCTTAGCAGCAAGAGC
ACCCCATGCTATATCTCCCCTGAGCTGTGTGAGGGCAAGCCCTACAACCAGAAGAGTGAC
ATCTGGGCCCTGGGCTGTGTCCTCTACGAGCTGGCCAGCCTCAAGAGGGCTTTCGAGGCT
GCGAACTTGCCAGCACTGGTGCTGAAGATCATGAGTGGCACCTTTTGCACCTATCTCTGAC
CGGTACAGCCCTGAGCTTCGCCAGCTGGTCCTGAGTCTACTCAGCCTGGAGCCTCCCAG
CGGCCACCACTCAGCCACATCATGGCACAGCCCCTCTCAACCACCCC
CACACCGACGGCAGAAGAGTCCGTGGCCCCCCAGCAACACAGGGAGCAGGACCACCAGTGT
CCGCTGCAGAGAGAGGCATCATCATGACATTCGGCAGCGGAGCAGAACACAGGGAGCCCCTAAGGCCCT

PCT/US00/14842

#### **FIGURE 2GGGG**

GGCAGCCTCACTGACATCAGCCAGCCCACCATTGTGGAGGCTTTGTTGGGCTATGAAATG GTGCAGCAAGTGGAGGAGGCCCTGAGCTTCACACTACTAGGCTCTGCACCCCTGGACCAG GAGCCTCTGCTGAGTATAGACCTGGGCACTGCTCACTCAGCTGCTGTGACTGGTGAGGAG GGTGTGGCGTCCAGCACTGATGTGTCTACCTTCTCTGAAGGTGACTGCAAGGAGCCTGAC AAGTGCTGCTGGAGACACAAGCAGTGCACTGGGCACATCATCTACCCTTTCGCCTCTGAC TGTGTCCGCCACAGCCTGCACCTACACTCTGTCAACCACTGCAACTGTAATTCTAGGCTG AAGGACTCTTCAGAGGATAGCAGCAGCTCCCGGGGCGCGGGCCCAACCTGCTCCCATGTC ATCGAGTCCCCTTGCTTTGAGCTCACACCGGAGGAGGAGCATGTGGAGCGATTCCGGTAT GGCTGGTGCAAAAGCTACAGACCTGTCTCTGTGGCAGTGATCCACCATCCACTCTACCAT GAGTGTGGGGCAGATGATCTAAATGXXAAGAAGAGGAAGAGGAGGAGGAGGAAAAGCAAG CCCCCATCCGACACAGGTGGGGCCCGCCACCGCCTCCCCTGACCTAGGCACCAGCATG GCCACTGGTACCCCTGACTCCACAGCGCCCATCACCATCTGGCGCTCTGAGAGCCCCACA GGGAAGGTCAGGGCAGCAAGGTGATCAAGAAGGTAAAGAAGAAAAAGGAAAAAGAGAAA GACAAGGAGGAGATGGATGAGAAGGCAAAGCTGAAGAAAAAAGCCAAGAAAGGCCAGTTG ACTAAGAAGAAAGCCCGGTTAAATTGGAGCCTTCCCCGCCAGACGTGAGCCGATCATTA AGCGCAAGACAGCTGGCCAGGATGTCCGAGTCCAGCCCAGAAAGCCGGGAAGAGCTGGAG AGCGAGGACAGTTACAATGGCCGGGGGCAGGAGAACTGTCCAGCGAGGATATTGTGGAA TCATCATCGCCCAGGAAGAGAGAGACACAGTCCAGGCCAAAAAGACAGGGGCAAAGCCC TCACAAGCCAGGAAGGTAAACAAGAGAAAATCTCCCCCAGGATCAAACCCCAACCTCAGT TGCTGTTCTCTCCCTCCAACCTGGCTGTTTCTTGCGGGGCAAGGGGTGGGCTCAGGGCTG CAGGGGTTTCTCAAAGGCAATCCAGCTTTCACAAAGGAAGCCCATGGGAAGGCAGGTGGG AGGGAAAGGAAGGGCACAGCCCTATTTCTTCCTACCTGCTAGGACAAGGTGGAAGAGTG TATCTGGGGTGGGAAGGAGGCTTCCCCTCTCTGCTGCAGAGACTGGTCTGTGAAAT CCACTTCTGGGACAGGCAGTACTGTCTGCAGCGATACCCCCAATAAACGGAACTTTTTAA CCC

SEO ID NO: 113 AA836348 H

ATGTCGGTGCTGGGCGAGTACGAGCGACACTGCGATTCCATCAACTCGGACTTTGGGAGC GAGTCCGGGGGTTGCGGGGACTCGAGTCCGGGGCCTAGCGCCAGTCAGGGGCCGCGAGCC GGCGCGCGCGCGGGGAGCAGGAGGAACTGCACTACATCCCCATCCGCGTCCTGGGCCGC GGCGCCTTCGGGGAAGCCACGCTGTACCGCCGCACCGAGGATGACTCACTGGTTGTGG AAGGAAGTCGATTTGACCCGGCTGTCTGAGAAGGAACGTCGTGATGCCTTGAATGAGATA GTTATTCTGGCACTGCTGCAGCACGACAACATTATTGCCTACTACAATCACTTCATGGAC AATACCACGCTGCTGATTGAGCTGGAATATTGTAATGGAGGGAACCTGTATGACAAAATC CTTCGTCAGAAGGACAAGTTGTTTGAGGAAGAGATGGTGGTGGTACCTATTTCAGATT GTTTCAGCAGTGAGCTGCATCCATAAAGCTGGAATCCTTCATAGAGATATAAAGACATTA AATATTTTCTGACCAAGGCAAACCTGATAAAACTTGGAGATTATGGCCTAGCAAAGAAA CTTAATTCTGAGTATTCCATGGCTGAGACGCTTGTGGGAACCCCATATTACATGTCTCCA GAGCTCTGTCAAGGAGTAAAGTACAATTTCAAGTCTGATATCTGGGCAGTTGGCTGCGTC ATTTTGAACTGCTTACCTTAAAGAGGACGTTTGATGCTACAAACCCACTTAACCTGTGT GTGAAGATCGTGCAAGGAATTCGGGCCATGGAAGTTGACTCTAGCCAGTACTCTTTGGAA TTGATCCAAATGGTTCATTCGTGCCTTGACCAGGATCCTGAGCAGAGACCTACTGCAGAT GAACTTCTAGATCGCCCTCTTCTCAGGAAACGCAGGAGGTCAAGCACTGTGACTGAAGCA CCCATTGCTGTAGTAACATCACGAACCAGTGAAGTCTATGTTTGGGGTGGTGGAAAATCC ACCCCCAGAAACTGGATGTTATCAAGAGTGGCTGTAGTGCCCGGCAGGTCTGTGCAGGG AATACCCACTTTGCTGTGGTCACAGTGGAGAAGGAACTGTACACTTGGGTGAACATGCAA GGAGGCACTAAACTCCATGGTCAGCTGGGCCATGGAGACAAAGCCTCCTATCGACAGCCA AAGCATGTGGAAAAGTTGCAAGGCAAAGCTATCCGTCAGGTGTCATGTGGTGATGATTTC

SEQ ID NO: 114 R86668 H, MKK6 H

#### FIGURE 2HHHH

ACTGTCTGTGTGACTGATGAGGGTCAGCTCTATGCCTTCGGATCAGATTATTATGGCTGC ATGGGGGTGGACAAAGTTGCTGGCCCTGAAGTGCTAGAACCCATGCAGCTGAACTTCTTC CTCAGCAATCCAGTGGAGCAGGTCTCCTGTGGAGATAATCATGTGGTGGTTCTGACACGA AACAAGGAAGTCTATTCTTGGGGCTGTGGCGAATATGGACGACTGGGTTTGGATTCAGAA GAGGATTATTATACACCACAAAAGGTGGATGTTCCCAAGGCCTTGATTATTGTTGCAGTT CAATGTGGCTGTGATGGGACATTTCTGTTGACCCAGTCAGGCAAAGTGCTGGCCTGTGGA CTCAATGAATTCAATAAGCTGGGTCTGAATCAGTGCATGTCGGGAATTATCAACCATGAA GCATACCATGAAGTTCCCTACACAACGTCCTTTACCTTGGCCAAACAGTTGTCCTTTTAT AAGATCCGTACCATTGCCCCAGGCAAGACTCACACAGCTGCTATTGATGAGCGAGGCCGG CTGCTGACCTTTGGCTGCAACAAGTGTGGGCAGCTGGGCGTTGGGAACTACAAGAAGCGT CTGGGAATCAACCTGTTGGGGGGACCCCTTGGTGGGAAGCAAGTGATCAGGGTCTCCTGC GGTGATGAGTTTACCATTGCTGCCACTGATGAGAAAGTATTGAATTCTAAGACCATCCGT TCCAATAGCAGTGGCTTATCCATTGGAACTGTGTTTCAGAGCTCTAGCCCGGGAGGAGGC GGCGGGGGCGGCGTGGTGAAGAAGAGGACAGTCAGCAGGAATCTGAAACTCCTGACCCA AGTGGAGGCTTCCGAGGAACAATGGAAGCAGACCGAGGAATGGAAGGTTTAATCAGTCCC GAGCTGGAAAATGCAGAATTTATCCCCATGCCTGACAGCCCATCTCCTCTCAGTGCAGCG TTTTCAGAATCTGAGAAAGATACCCTGCCCTATGAAGAGCTGCAAGGACTCAAAGTGGCC TCTGAAGCTCCTTTGGAACACAAACCCCAAGTAGAAGCCTCGGTAACTGAGCTTTTTGCC TTTGAATCACAACTAGTCACCTCGGCTGAATCCTGCAGTAACCTGTGCTGGGAAGGGAAC ACCACTGACTCCTCCTGCGTGTGCGTGCAGCTCTCTGCAGGTGGAGGTTGA

GAGACGCTGCAGGCCTTGCCCACCTGTGATGTGGCCGAGCAGCATAATGTCTGCTTCCAC CTGCTGCCGCTGGTACAGCTTGAGGGCTCTGTGGCGCCCCGATCTGTACTGCATGTGTGGC CGTATCTACAAGGACATGTTCTTCAGCTCGGGTTTCCAGGATGCTGGGCACCGGGAGCAG GCCTATCACTGGTATCGCAAGGCTTTTGACGTAGAGCCCAGCCTTCACTCAGGCATCAAT GCAGCTGTGCTCATTGCTGCCGGCAGCACTTTGAGGATTCCAAAGAGCTCCGGCTA ATAGGCATGAAGCTGGGCTGCCTGCTGGCCCGCAAAGGCTGCGTGGAGAAGATGCAGTAT GTGCTGGCTGCAGAGCAGCTGTATAAGCTCAATGCCCCCATATGGTACCTGGTGTCCGTG ATGGAGACCTTCCTGCTCTACCAGCACTTCAGGCCCACGCCAGAGCCCCCTGGAGGGCCA CCACGCCGTGCCCACTTCTGGCTCCACTTCTTGCTACAGTCCTGCCAACCATTCAAGACA GCCTGTGCCCAGGGCGACCAGTGCTTGGTGCTGGTCCTGGAGATGAACAAGGTGCTGCTG CCTGCAAAGCTCGAGGTTCGGGGTACTGACCCAGTAAGCACAGTGACCCTGAGCCTGCTG GAGCCTGAGACCCAGGACATTCCCTCCAGCTGGACCTTCCCAGTCGCCTCCATATGCGGA GTCAGCGCCTCAAAGCGCGACGAGCGCTGCTGCTTCCTCTATGCACTCCCCCCGGCTCAG GACGTCCAGCTGTGCTTCCCCAGCGTAGGGCACTGCCAGTGGTTCTGCGGCCTGATCCAG GCCTGGGTGACGAACCCGGATTCCACGGCGCCCGCGGAGGAGGCGGAGGGCGCGGGGGAG ATGTTGGAGTTTGATTATGAGTACACGGAGACGGCCGAGCGGCTGCTGCCAAGGGC ACGTATGGGGTGTACGCGGGCCGCGATCGCCACACGAGGGTGCGCATCGCCATCAAG GAGATCCCGGAGCGGGACAGCAGGTTCTCTCAGCCCCTGCATGAAGAGATCGCTCTTCAC AGACGCCTGCGCCACAAGAACATAGTGCGCTATCTGGGCTCAGCTAGCCAGGGCGGCTAC 

TGGGGACCCCTGAAGGACAACGAGAGCACCATCAGTTTCTACACCCGCCAGATCCTGCAG GGACTTGGCTACTTGCACGACAACCACATCGTGCACAGGGACATAAAAGGGGACAATGTG CTGATCAACACCTTCAGTGGGCTGCTCAAGATTTCTGACTTCGGCACCTCCAAGCGGCTG GCAGGCATCACACCTTGCACTGAGACCTTCACAGGAACTCTGCAGTATATGGCCCCAGAA

ATGAACTTGCTGCTCTCCTACCGCGATGTGCAGGACTACTCGGCCATCATTGAGCTGGTG

#### FIGURE 2IIII

ATCATTGACCAGGGCCCACGCGGGTATGGGAAAGCAGCTGACATCTGGTCACTGGGCTGC ACTGTCATTGAGATGGCCACAGGTCGCCCCCCTTCCACGAGCTCGGGAGCCCACAGGCT GCCATGTTTCAGGTGGGTATGTACAAGGTCCATCCGCCAATGCCCAGCTCTCTGTCGGCC GAGGCCCAAGCCTTTCTCCTCCGAACTTTTGAGCCAGACCCCCGCCTCCGAGCCAGCGCC CAGACACTGCTGGGGGACCCCTTCCTGCAGCCTGGGAAAAGGAGCCGCAGCCCCAGCTCC CCACGACATGCTCCACGGCCCTCAGATGCCCCTTCTGCCAGTCCCACTCCTTCAGCCAAC CCCCGAAGCGCTGCCTCAGTTATGGGGGCACCAGCCAGCTCCGGGTGCCCGAGGAGCCT GCGGCCGAGGAGCCTGCGTCTCCGGAGGAGAGTTCGGGGCTGAGCCTGCTGCACCAGGAG AGCAAGCGTCGGGCCATGCTGGCCGCAGTATTGGAGCAGGAGCTGCCAGCGCTGGCGGAG AATCTGCACCAGGAGCAGAAGCAAGAGCAGGGGGCCCGTCTGGGCAGAAACCATGTGGAA GAGCTGCTGCGCTCGGGGCACACATCCACACTCCCAACCGCCGGCAGCTCGCCCAG GAGCTGCGGGCGCTGCAAGGACGGCTGAGGGCCCAGGGCCTTGGGCCTGCGCTTCTGCAC AGACCGCTGTTTGCCTTCCCGGATGCGGTGAAGCAGATCCTCCGCAAGCGCCAGATCCGT CCACACTGGATGTTCGTTCTGGACTCACTGCTCAGCCGTGCTGTGCGGGCCAGCCCTGGGT GTGCTAGGACCGGAGGTGGAGAAGGAGGCGGTCTCACCGAGGTCAGAGGAGCTGAGTAAT GAAGGGGACTCCCAGCAGAGCCCAGGCCAGCAGCAGCCCGCTTCCGGTGGAGCCCGAGCAG GGCCCGCTCTCTGATGGTGCAGCTGAGCCTCTTGAGGGCAGAGACTGATCGGCTGCGC GAAATCCTGGCGGGAAGGAACGGGAGTACCAGGCCCTGGTGCAGCGGGCTCTACAGCGG CTGAATGAGGAAGCCCGGACCTATGTCCTGGCCCCAGAGCCTCCAACTGCTCTTTCAACG GACCAGGGCCTGGTGCAGTGGCTACAGGAACTGAATGTGGATTCAGGCACCATCCAAATG CTGTTGAACCATAGCTTCACCCTCCACACTCTGCTCACCTATGCCACTCGAGATGACCTC ATCTACACCCGCATCAGGGGAGGGATGGTATGCCGCATCTGGAGGGCCATCTTGGCACAG CGAGCAGGATCCACACCAGTCACCTCTGGACCCTGA

SEQ ID NO: 115 PAK6 H

ATGTTTGGGAAGAAAAGAAAAGATTGAAATATCTGGCCCGTCCAACTTTGAACACAGG GTTCATACTGGGTTTGATCCACAAGAGCAGAAGTTTACCGGCCTTCCCCAGCAGTGGCAC AGCCTGTTAGCAGATACGGCCAACAGGCCAAAGCCTATGGTGGACCCTTCATGCATCACA TCCATCAACGGCCTGCTAGAGGATTTTGACAACATCTCGGTGACTCGCTCCAACTCCCTA AGGAAAGAAGCCCACCCACCCAGATCAGGGAGCCTCCAGCCACGGTCCAGGCCACGCG GAAGAAAATGGCTTCATCACCTTCTCCCAGTATTCCAGCGAATCCGATACTACTGCTGAC TACACGACCGAAAAGTACAGGGAGAAGAGTCTCTATGGAGATGATCTGGATECGTATTAT AGAGGCAGCCAGCCAAGCAAAATGGGCACGTAATGAAAATGAAGCACGGGGAGGCC TACTATTCTGAGGTGAAGCCTTTGAAATCCGATTTTGCCAGATTTTCTGCCGATTATCAC TCACATTTGGACTCACTGAGCAAACCAAGTGAATACAGTGACCTCAAGTGGGAGTATCAG AGAGCCTCGAGTAGCTCCCCTCTGGATTATTCATTCCAATTCACACCTTCTAGAACTGCA GGGACCAGCGGGTGCTCCAAGGAGACCTGGCGTACAGTGAAAGTGAATGGGGACCCAGC CTGGATGACTATGACAGGAGGCCAAAGTCTTCGTACCTGAATCAGACAAGCCCTCAGCCC ACCATGCGGCAGAGGTCAGGTCAGGCTCGGGACTCCAGGAACCGATGATGCCATTTGGA GCAAGTGCATTTAAAACCCATCCCCAAGGACACTCCTACAACTCCTACACCTACCCTCGC TTGTCCGAGCCCACAATGTGCATTCCAAAGGTGGATTACGATCGAGCACAGATGGTCCTC AGCCCTCCACTGTCAGGGTCTGACACCTACCCCAGGGGCCCTGCCAAACTACCTCAAAGT CAAAGCAAATCGGGCTATTCCTCAAGCAGTCACCAGTACCCGTCTGGGTACCAAAAGCC ACCTTGTACCATCACCCCTCCCTGCAGAGCAGTTCGCAGTACATCTCCACGGCTTCCTAC CTGAGCTCCCTCAGCCTCTCATCCAGCACCTACCCGCCCCAGCTGGGGCTCCTCCTCC GACCAGCAGCCTCCAGGGTGTCCCATGAACAGTTTCGGGCGGCCCTGCAGCTGGTGGTC AGCCCAGGAGACCCCAGGGAATACTTGGCCAACTTTATCAAAATCGGGGAAGGCTCAACC GGCATCGTATGCATCGCCACCGAGAAACACACAGGGAAACAAGTTGCAGTGAAGAAAATG WO 00/73469 PCT/US00/14842

#### FIGURE 2JJJJ

SEQ ID NO: 116 SURTK106 H ATGAATGATAGGAATGAGATTCAAATGGAAGCCAAACTCCAAAGTCTTACCATTATAGCA CAGGAAATTCTATGCAGATTCTTTATTACCCTTAGGAGACATGCACGTTTCCTGCTCACT AAACTAGGAAGGCAAGGAATGGCAAGGTCAGGAATTACTCACAGCTGTGCTGTGCATT CTCTGTGGGCCTAGCAGGGAAGGGGACAGCCCTGTGGCAATGGGCATGACACGGATGCTC CTGGAATGCAGTCTCAGTGACAAGTTGTGTCTCATCCAGGAGAAGCAGTATGAAGTGATT ATCGTCCCAACTTTGTTGGTTACTATCTTCCTCATCCTTCTTGGGGTCATCCTGTGGCTT TTTATCAGAGAACAAAGAACTCAACAGCAGCGTTCTGGACCTCAAGGCATTGCCCCTGTT CCTCCACCTAGGGACCTAAGCTGGGAAGCAGGACATGGAGGAAATGTGGCTTTGCCACTT AAGGAGACATCCGTGGAAAACTTTCTGGGAGCTACCACACCTGCCCTGGCTAAGCTGCAG GTGCCGCGGGAGCAACTCTCTGAAGTTCTGGAGCAGATTTGCAGTGGTAGCTGTGGGCCC ATCTTTCGAGCCAATATGAACACTGGGGACCCTTCTAAGCCCAAGAGTGTTATTCTCAAG GCTTTAAAAGAACCAGCTGGGCTCCATGAGGTACAAGATTTCTTAGGGCGAATCCAATTC CATCAATACCTGGGGAAACACAAAAACCTGGTGCAGCTGGAAGGCTGCTGCACTGAAAAG CTGCCACTCTATATGGTGTTGGAGGATGTGGCCCAGGGGGACCTGCTCGGCTTTCTCTGG ACCTGTCGGCGGGATGTGATGACTATGGATGGTCTTCTCTATGATCTCACAGAAAAACAA GTATATCACATCGGAAAGCAAGTCCTTTTGGCGCTGGAATTCCTGCAGGAGAAGCATTTG TTCCATGGGGATGTGGCAGCCAGGAATATTCTGATGCAAAGTGATCTCACTGCTAAGCTC TGTGGATTAGGCCTGGCTTATGAAGTTTACACCCGAGGGGCCATCTCCTCTACTCAAACC ATACCTCTCAAGTGGCTTGCCCCAGAACGGCTTCTCCTGAGACCTGCTAGCATCAGAGCA GATGTCTGGTCTTTTGGGATCCTGCTCTATGAGATGGTGACTCTAGGAGCACCACCGTAT CCTGAAGTCCCTCCTACCAGCATCCTAGAGCATCTCCAAAGAAGGAAAATCATGAAGAGA CCCAGTAGCTGCACACATACCATGTACAGTATCATGAAGTCCTGCTGGCGTGGCGTGAG GCTGACCGCCCTCACCTAGAGAGCTGCGCTTGCGCCTAGAAGCTGCCATTAAAACTGCA GATGACGAGGCTGTGTTACAAGTACCAGAGTTGGTGGTACCTGAACTGTATGCAGCTGTG GCCGGCATCAGAGTGGAGAGCCTCTTCTACAACTATAGCATGCTTTGAAGAGTCTCGGGC AAGAAACATTCATGCATGAGTATATGTTCTTGGAATCAATTCCTCTAAGAACAGAGAATG GTCTTTCCCAGGGACACAAAGGGAGAAATGGGACATGGATTCTTGATCTTCCTTTACACA TTTCTCGGGAAATCTGAAATGATGCTGGATGGGACTCTACACATCCTGAGCTAAGACATA CTGTCAGTCTCACTTCTGCTGTCCCAGTCCTAGAAATCCTGGGTAGAAGTGGTGGACCTG TGCAAAGGAGGTTTTAGAACTCTGCAGTATTTGTTGGGGCATGGCACAAATAAGCTCATC CCTCCCGTCCGAGGCTAGTTTCCTCTGGAACCACATTTTTATCTAGATGAAAATTTGGAA CTTGCTCAGGATTACAGATATGGACCAACACCTCCTTCAAGAAAAGGTGGTAGGACACAA AGTTCTTCAGTCCTGAGCCCTACATGTGGGGGCTGGAGGAGAACTATAACGGAAAAACCTC TGAGTTTCACCTTAGGTATAGATAAAAGAAAGATGGTCCCCTTTTATCTGATTCTGAGAC AGGTAAATTCTGTTTGTTACTACGTTTAATTAGAAGGTGGAGGAGTCATTTCATGATTAA

#### FIGURE 2KKKK

SEO ID NO: 117 AA098024 M CTGCAGGAGAAGCACCTGTTTCATGGGGATGTGGCTGCCAGGAACATCCTGATCCAAAGT GACCTGACTCCCAAACTTTGTCATCTGGGCCTGGCTTATGAAGTTCATGCCCATGGGGCC ATCTCCTCTGCTCGATCCAGCACCATCCCTCTCAAGTGGCTTGCTCCAGAAAGGCTTCTC CTGAGACCTGCAAGCATCAGGGGAGATATTTGGTCCTTTGGGATCCTGCTTTATGAGATG GTGACTCTAGGAGCACCACCATACCCTGAAGTCCCTCCCACCAGCATCCTACAATATCTT CAGAGAAAGAAATCATGAAGAGACCCAGCAGCTGCTCACATGCCATGTACAACATCATG AAGTGCTGTTGGCGCTGGAGTGAGGACAGCCGCCCCTTACTTGTTCAGCTGCTCCAGCGC CTAGAAGCTGCTTCTAGATCTGCCGATGACAAGGCTGTGTTGCAAGTGCCAGAGTTGGTG GTGCCTGAACTGTATGCAGATGTGGCTGGCATCAGGGCAGAAAGCATTTCCTATAGCTTC AGTGTCCTTTGAAGATGGTCCTAGACAAATGACTATATATGGGTGGAATTAGTTCCTTCA AGAACAGAGAAGGAACTTTCTGTGGCCCACCAAGGGAGAAAAAAGGACATGGATCTTG CATCTTTCCCTAAACATTTTCCTAGACATCTGAAATGCTGCTGGATGAAGCTCTACCTCT ACATACCATGTACTCTTGAGCTAAGAATCACCATCAATTGTAGTTTGCTTTTCCAGTCCCA AGGGCTGAAGTATAAGTGGTGGACCGTGTCATTCTAAAGGAGGTTTTTAAAATCTGCAAT AAACTAGTTTTCTTTTTTTTTTTTAAGTTAAACTATTACAGAGTAAAAATAAACCAG ATGGGCATGAATGAACACCTTCTAATTTTTAACCATGAATTGAATATTGGAATTCATGAG AAAGAAAATTCTAGGTTCTTTTTGCTAAGAGGTGTTAAGGTGAGTCAATATATCCTTCAA GGAAAGGCTTTGTCTCATCTATGTTGACGGGACGTAAAAGTCCTCGTCCCGTTATGAAGA TCCTTTCATTGAACTCTGAGGCAGGTGGACCATGCATGATACTAAGTTTAATTAGAAGCA GTATAACAAATAGGAAGCATGAAAGTCGAGCAAGAAGACTTAGTAACCCAGGTGGTCATT GTTATTTTACTAGGAAAATTAGAGAACCTATAGTTTCCAAAAAGAGATTCTTTATGTGCA AAATGAGATAACTCTCTACCTCACAGGGTTGGTGTGAGGAACAATGAGAATATGTATTTG TGTATTATGTAGAATATAATATTCTCAATAAATACTAGTTTTTCCCCCTTTC

## FIGURE 2LLLL

TCCACATTCTGTGGTACCCCTGAGTACTTGGCACCTGAAGTGCTTCGGAAAGAGCCTTAT GATCGAGCAGTGGACTGGTGGTGCTTGGGGGCCAGTCCTCTACGAGATGCTCCATGGCCTG CCGCCCTTCTACAGCCAAGATGTATCCCAGATGTATGAGAACATTCTGCACCAGCCGCTA CAGATCCCCGGAGGCCGGACAGTGGCCGCCTGTGACCTCCTGCAAAGCCTTCTCCACAAG GACCAGAGGCAGCGGCTCCAAAGCAGACTTTCTTGAGATTAAGAACCATGTATTC TTCAGCCCCATAAACTGGGATGACCTGTACCACAAGAGGCTAACTCCACCCTTCAACCCA AATGTGACAGGACCTGCTGACTTGAAGCATTTTGACCCAGGAGTTCACCCAGGAAGCTGTG TCCAAGTCCATTGGCTGTACCCCTGACACTGTGGCCAGCAGCTCTGGGGCCTCAAGTGCA ACCTGTGAAACTACTGAGGCCAGCTGGTATTAGTAAGGAATTACCTTCAGCTGCTAGGAA GAGCGACTCAAACTAACAATGGCTTCAACGAGAAGCAGGTTTATTTTTTCCAGCACATAA AAGAAAAATAATGTTTCGGAGTCCAGGACTGGCAGGACAGGTCATCAGATACTCAGAGGC TGTATCTCTGCCCTGCCAACCTTGACAAATGGCTTCCAATGTTAGGTTTGCTACAAGATG GTTACTGGAGCTCTAGCTGCCTATTTTGTGTTTAGGGAAGGGAAAATGGAGGAAAGGGGA GAAGAGCAAAGGCCCCCCAATGACTTTTGCTT CCATCTCACTAACCACCCCACCCTACCTGGAATGGAGGCTGGGAAATGTGGCTTATTTGC TGGGTACGTGACTATCCCTAATAACAAGGGGTTTTGACCCTAAGACATTAGGGGAGAAT GTTGGGTAGGCAGCCAGCCCTCTTTTACCATAGGGCCTCCTGGTGTTTTGGATTTTGATCT CAATGTGTAAAATGACAGAGATGTAACAAGCTCATAGGGTATCAATATCTCTTATTGTTC TATGTTGAAAAA

SEQ ID NO: 120 CCRK H

ATGGACCAGTACTGCATCCTGGGCCGCATCGGGGAGGGCGCCCACGGCATCGTCTTCAAG GCCAAGCACGTGGAGACTGGCGAGATAATTGCCCTCAAGAAGGTGGCCCTAAGGCGGTTG GAAGACGGCTTCCCTAACCAGGCCCTGCGGGAGATTAAGGCTCTGCAGGAGATGGAGGAC AATCAGTATGTGGTACAACTGAAGGCTGTGTTCCCACACGGTGGAGGCTTTGTGCTGGCC TTTGAGTTCATGCTGTCGGATCTGGCCGAGGTGGTGCGCCATGCCCAGAGGCCACTAGCC CAGGCACAGGTCAAGAGCTACCTGCAGATGCTCAAGGGTGTCGCCTTCTGCCATGCC AACAACATTGTACATCGGGACCTGAAACCTGCCAACCTGCTCATCAGCGCCTCAGGCCAG CTCAAGATAGCGGACTTTGGCCTGGCTCGAGTCTTTTCCCCAGACGGCAGCCGCCTCTAC ACACACCAGGTGGCCACCAGGTCTGTGGGCTGCATCATGGGGGAGCTGTTGAATGGGTCC CCCCTTTCCCGGGCAAGAACGATATTGAACAGCTTTGCTATGTGCTTCGCATCTTGGGC ACCCCAAACCCTCAAGTCTGGCCGGAGCTCACTGAGCTGCCGGACTACAACAAGATCTCC TTTAAGGAGCAGGTGCCCATGCCCCTGGAGGAGGTGCTGCCTGACGTCTCTCCCCAGGCA TTGGATCTGCTGGGTCAATTCCTTCTCTACCCTCCTCACCAGCGCATCGCAGCTTCCAAG ATTCCTCAGCGTCTAGGGGGACCTGCCCCCAAGGCCCATCCAGGGCCCCCCCACATCCAT GACTTCCACGTGGACCGGCCTCTTGAGGGAGTCGCTGTTGAACCCAGAGCTGATTCGGCC TCAGTCCACCTGTTCCTCTGCCACCTGCCTGGCTTCACCCTCCAAGGCCTCCCCATGGCC ACAGTGGGCCCACACCACCTTGCCCCTTAGCCCTTGCGAGGGTTGGTCTCGAGGCAGA GGTCATGTTCCCAGCCAAGAGTATGAGAACATCCAGTCGAGCAGAGGAGATTCATGGCCT GTGCTCGGTGAGCCTTACCTTCTGTGTGCTACTGACGTACCCATCAGGACAGTGAGCTCT GAGTGCTGCCTCCTGGTCAAGGAGAAGTGCAGAGAGTAA

SEQ ID NO: 121 TESK2 H GAATTCGCGGCCGCTCGACGCTCAGCAGAGCTACCAGCTGCCCTGTTGGCTTCGCTGGTC

GGATCGTCCTCCTGGCCCCGCCAAACAGGCGAGCGGCCCCGACTGTGGGGCATGGCAGTA GTCTCCTCGTTCTCCGCCGCCGCTAGCCTAGCTGAGTCGCCGGCTTCTGCGCTAGGGGCT

#### **FIGURE 2MMMM**

CCCACCGCCTCCGCAGGCTAAGGAGCCGCTGCCACCAACGAGCTGTGAGGGTTACTATGC TCCCTCTTTGCCGCCGTCTCCTCTTGCCCGCGCAGGCACCCCTCTGGCTGCTCAGTC CTGCCTCAGTGTCAAACCAGAAGAAGTAAAATTCAACAAAAATTTATGTGTGGAGTTC CTTCTTAAAAGAAGAAAAAGTGATTATTTAGACTATGGATCGGAGCAAACGGAATTCAA TTGCAGGATTTCCTCCACGTGTGGAGCGTCTTGAAGAGTTTGAAGGAGGTGGTGGAGGAG AAGGAAATGTGAGCCAGGTGGGAAGAGTTTGGCCATCTTCGTATCGAGCTCTTATAAGTG CCTTTTCCAGACTGACGCGTTTGGATGATTTCACCTGTGAAAAAATAGGGTCTGGCTTCT TTTCTGAAGTGTTCAAGGTACGACACCGAGCTTCTGGTCAGGTGATGGCTCTTAAGATGA ACACATTGAGCAGTAACCGGGCAAACATGCTGAAAGAAGTACAGCTCATGAATAGACTCT CCCATCCCAACATCCTTAGGTATATCAACTCCGGGAACCTGGAACAGTTGCTAGACAGTA ACCTGCATTTGCCTTGGACTGTGAGGGTAAAACTGGCCTATGACATAGCAGTGGGCCTCA GCTACCTTCACTTCAAAGGCATTTTTCATCGGGACCTCACATCTAAGAACTGCCTGATAA AGAGGGATGAGAATGGTTACTCTGCAGTGGTAGCTGACTTTGGCCTGGCTGAGAAGATCC CCGATGTCAGCATGGGGAGTGAGAAGCTGGCCGTGGTGGGTTCCCCCATTCTGGATGGCAC CTGAGGTTCTCCGAGATGAGCCCTATAATGAAAAGGCAGATGTGTTCTCTTATGGTATCA TCCTCTGCGAGATCATCGCCCGCATCCAGGCCGATCCGGACTATCTTCCCCGCACAGAGA ATTTCGGGCTGGACTATGATGCTTTCCAGCACATGGTGGGAGACTGTCCCCCAGATTTTC TGCAACTTACTTTCAACTGCTGTAACATGGATCCCAAACTGCGCCCATCTTTTGTGGAGA TTGGGAAGACCCTGGAGGAAATTCTGAGCCGCCTACAGGAAGAAGAGCAGGAGAGGGATA GGAAGCTGCAGCCCACAGCCAGGGGACTCTTGGAGAAAGCACCTGGGGTGAAGCGACTAA GCTCACTGGATGACAAGATCCCCCACAAGTCACCATGCCCAAGACGTACCATCTGGCTGT CATACTACCGGCCACGAGATGGTGCTGCCCGCACCCCCAAAGTCAACCCTTTTAGTGCTC GCCAGGACCTCATGGGGGGCAAGATCAAGTTTTTTGACCTGCCCAGCAAGTCTGTCATCT CTCTGGTATTTGACCTGGATGCACCAGGGCCCGGAACTATGCCCCTGGCTGACTGGCAGG AGCCCCTGGCCCACCTATTCGCCGGTGGCGTTCCTTGCCTGGTTCGCCTGAGTTCTTGC ATCAAGAGGCTTGTCCATTTGTGGGCCGGGAAGAATCGCTATCTGATGGGCCCCCACCAC GCCTAAGTAGTCTCAAGTACAGAGTTAAAGAGATCCCACCATTCCGGGCATCTGCCCTAC CAGCTGCTCAAGCCCATGAGGCTATGGACTGCTCCATTCTCCAGGAAGAAAATGGTTTTG GGTCCAGGCCCCAGGGGACCAGTCCATGCCCTGCGGGTGCTTCTGAGGAGATGGAGGTAG AAGAAAGGCCAGCAGCTCAACTCCAGCCACCTTCTCCACCTCAGGCATAGGCCTGCAAA CCCAGGGAAAGCAGGATGGGTGAGGGGGTTTAGTCCCTGCCTCACCTTGGGGATGGACCT TCAGCTGAAACCATATGGCCCCCTAGGTGCACAGCCTTGATTCTTCCCTGGAGCCTACAG AGCAGGCAGGCTAGGCCAAGCCAGGCTCAACTTCTGGGCTCCCAGTGCCCATTGGCTGTG TATGACGGGAGCAGCAGTGAGAGGCCTTCCTAGTTAGGGCCAACAGCTGATACCAAGCC TCTGAAATCCAGCAAGGAGGTCTGCCTCCCACCAGACCCTCTCCAGTGTACTTCCCCAGA TCCCCACCCCAGGTCTGTCTTTGCCTTTTCTTGGGGCATATAAGCTACTGAGTGGAACA TGGAGCTGATCAAGAGGCCGTAATGGTCATGGCTGTTTCCAGACCTGAATATTGGGTGCT TCTTGCCAGTATTCTAAGACATTTGAGTAATTGCTGTTTTGCACTTACTGCATGGTCAGAC CACGTCACTACATTTCTATGCAAGGGGACAGCAAGGCAGCGTGGTGGTCATGGCTCTTAG CTAACCTATTCAAAGACCTTTTCCTGTTGATTAATCTATTTTCATATTTATAAAGGAGTC TTAATGTTCTGCCCCATAAGACTTTCAACCTTGTGGTTGGGAGTGGGGCTGGTTTTGTAG GCCCTAGGGCCTGCTTCTATGTATTTATCAACATGTGATACATTCAATTGGTTAAATGGT TTATACAGGGACTGATTTGCTTCCCTTCCTGCCATGGCTGGAGCTTTGGGAACAGTCTGT CCTTACAGAGCTGCAATAAGAAATAACCAAAGATGAAGCTGGTCAAATATTTTCATAACT TGCTTCTGTTGATTTTTTTTTTTGTAAAACTTTCCCAAGACATTTTCAGACTTAAAAATAA AGTCAGTGTTACAGGT

THIS PAGE BLANK (USPTO)

# (19) World Intellectual Property Organization International Bureau





(43) International Publication Date 7 December 2000 (07.12.2000)

**PCT** 

(10) International Publication Number WO 00/73469 A3

- (51) International Patent Classification<sup>7</sup>: C12N 15/54, 9/12, 15/11, 5/12, C07K 16/40, A61K 38/00, G01N 33/68
- (21) International Application Number: PCT/US00/14842
- (22) International Filing Date: 26 May 2000 (26.05.2000)
- (25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

60/136,503

28 May 1999 (28.05.1999) US

- (71) Applicant (for all designated States except US): SUGEN, INC. [US/US]; 230 East Grand Avenue, South San Francisco, CA 94080 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): PLOWMAN, Gregory, D. [US/US]: 4 Honeysuckle Lane, San Carlos, CA 94070 (US). MARTINEZ, Ricardo [US/US]; 984 Cartier Lane. Foster City, CA 94404 (US). WHYTE, David [US/US]; 2623 Barclay Way. Belmont, CA 94002 (US). SUDERSANAM, Sucha [US/US]; 20 Corte Patencio, Greenbrae, CA 94904 (US).

- (74) Agent: FOLEY & LARDNER: Suite 500, 3000 K Stret. N.W., Washington, D.C. 20007-8696 (US).
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
- (84) Designated States (regional): ARIPO patent (GH. GM. KE. LS. MW. MZ. SD. SL. SZ. TZ. UG. ZW). Eurasian patent (AM. AZ. BY. KG. KZ. MD. RU. TJ. TM), European patent (AT. BE. CH. CY. DE. DK. ES. FI. FR. GB. GR. IE, IT. LU. MC. NL. PT. SE). OAPI patent (BF. BJ. CF. CG. CI. CM. GA. GN. GW. ML. MR. NE, SN. TD. TG).

#### Published:

with international search report

(88) Date of publication of the international search report: 29 November 2001

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

0/73469 A3

(54) Title: PROTEIN KINASES

(57) Abstract: The present invention relates to kinase polypeptides, nucleotide sequences encoding the kinase polypeptides, as well as various products and methods useful for the diagnosis and treatment of various kinase-related diseases and conditions.

PCT/US 00/14842

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/54 C12N C12N9/12 C12N15/11 C12N5/12 CO7K16/40 A61K38/00 G01N33/68 According to International Patent Classification (IPC) or to both national classification and IPC B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) IPC 7 C12N C07K A61K G01N Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, WPI Data, PAJ, EMBL, MEDLINE, BIOSIS C. DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. X DATABASE EMBL 'Online! 2,6,7, accession number W65887 11,12 12 June 1996 (1996-06-12) MARRA M. ET AL.: "The WashU-HHMI mouse EST project." XP002157499 abstract DOC. AGAINST INV. 1 (SEQ.IDs. 122, 4) WO 00 58473 A (CURAGEN CORP ; LEACH MARTIN Ε 1,2,4-7(US); SHIMKETS RICHARD A (US)) 11.12 5 October 2000 (2000-10-05) SEQ.IDs. 4435 and 4436 DOC. AGAINST INV. 1 (SEQ.IDs. 122, 4) SEQ.IDs. 5049, 5050, 5571, 5572 DOC. AGAINST INV. 67 (SEQ.IDs. 188, 70) SEQ.IDs. 3009 and 3010 DOC. AGAINST INV. 76 (SEQ.IDs. 197, 79) X Further documents are listed in the continuation of box C. Patent family members are listed in annex. Special categories of cited documents: \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the "A" document defining the general state of the art which is not considered to be of particular relevance invention "E" earlier document but published on or after the international "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such docu-ments, such combination being obvious to a person skilled in the art. "O" document referring to an oral disclosure, use, exhibition or \*P\* document published prior to the international filing date but later than the priority date claimed "&" document member of the same patent family Date of the actual completion of the international search Date of mailing of the international search report 18. 07. 2001 22 June 2001 Name and mailing address of the ISA Authorized officer European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040. Tx. 31 651 epo ni, Mandl, B Fax: (+31-70) 340-3016

Form PCT/ISA/210 (second sneet) (July 1992)

Int aional Application No PCT/US 00/14842

<u> </u>	Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
ategory ° C	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	
P,X	RUIZ-PEREZ V. L. ET AL.: "Mutations in a new gene in Ellis-van Creveld syndrome and Weyers acrodental dysostosis."  NATURE GENETICS, vol. 24, no. 3, March 2000 (2000-03), pages 283-286, XP002157498  ISSN: 1061-4036 page 284, left-hand column, line 6 - line 8  figure 1A page 286, right-hand column, last paragraph & DATABASE EMBL 'Online! Accession Number Q9NY57, 1 October 2000 (2000-10-01)  PUIZ-PEREZ V. V. ET AL.: "Serine/threonine protein kinase." abstract DOC. AGAINST INV. 1 (SEQ.IDs. 122, 4)	1-12	
	DATABASE EMBL 'Online! Accession NumberAA305176, 18 April 1997 (1997-04-18) ADAMS M. D. ET AL.: "EST176172 colon carcinoma cell line II Homo sapiens cDNA 5'-end." XP002165842 abstract DOC. AGAINST INV. 3 (SEQ.IDs. 124, 6)	6,7	
	DATABASE EMBL 'Online! Accession Number AA116841, 16 November 1996 (1996-11-16) MARRA M. ET AL.: "Mus musculus cDNA clone IMAGE:538568 5' similar to TR:G406058 protein kinase." XP002165843 abstract DOCAGAINST_INV. 4_(SEQ.IDs. 125,_7)	1,2,4,6, 7,10-13, 15	
P,X	WO 00 06728 A (INCYTE PHARMA INC; PATTERSON CHANDRA (US); AZIMZAI YALDA (US); COR) 10 February 2000 (2000-02-10)  SEQ.ID.1 and 32 DOC. AGAINST INV. 4 (SEQ.IDs. 125, 7)	2,4-7,9, 11-14, 26,27, 35,36	
X	WO 98 58052 A (INCYTE PHARMA INC ;CORLEY NEIL C (US); BANDMAN OLGA (US); GOLI SUR) 23 December 1998 (1998-12-23) SEQ.IDs. 4 and 11 DOC. AGAINST INV. 5 (SEQ.IDs. 126, 8)	1-14, 26-30, 35-38	

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

Int tional Application No PCT/US 00/14842

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT  Category Citation of document, with indication where appropriate of the relevant passages.			
calegory °	Citation of document, with indication where appropriate, of the relevant passages	Relevant to claim No.	
E	WO 00 55332 A (INCYTE PHARMA INC; AZIMZAI YALDA (US); YUE HENRY (US); AU YOUNG JA) 21 September 2000 (2000-09-21) SEQ.IDs. 7 and 21 DOC. AGAINST INV. 6 (SEQ.IDs. 127, 9) SEQ.IDs. 2 and 16 DOC. AGAINST INV. 26 (SEQ.IDs. 147, 29)	1-15, 26-30, 35-38	
X	DATABASE EMBL 'Online! Accession Number AA593989, 24 September 1997 (1997-09-24) STRAUSBERG R.: "Homo sapiens clone IMAGE:1084047 3' similar to TR:G20878 serine/threonine protein kinase." XP002165844 abstract DOC. AGAINST INV. 6 (SEQ.IDs. 127, 9)	1,2,4,6, 7,10-13, 15	
X	DATABASE EMBL 'Online! Accession Number AL050147, 20 May 1999 (1999-05-20) WAMBUTT R. ET AL.: "Homo sapiens mRNA." XP002165845 abstract DOC. AGAINST INV. 6 (SEQ.IDs. 127, 9)	6,7	
X	HAYASHI A. ET AL.: "PKCnu, a new member of the protein kinase C family, composes a fourth subfamily with PKCmu." BIOCHIMICA ET BIOPHYSICA ACTA, vol. 1450, no. 1, 6 May 1999 (1999-05-06), pages 99-106, XP000992627 ISSN: 0006-3002 the whole document DOC. AGAINST INV. 8 (SEQ.IDs. 129, 11)	1-15, 35-38	
X	DATABASE EMBL 'Online! Accession Number AA763046, 28 January 1998 (1998-01-28) MARRA M. ET AL.: "Mus musculus cDNA clone similar to TR:P70268 protein kinase." XP002165846 abstract DOC. AGAINST INV. 9 (SEQ.IDs. 130, 12)/	2,6,7, 11,12	

16

Form PCT/ISA/210 (continuation of second sneet) (July 1992)

Int .tional Application No
PCT/US 00/14842

	INION) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Ρ,Χ	OISHI K. ET AL.: "Identification and characterization of PKNbeta, a novel isoform of protein kinase PKN: Expression and arachidonic acid dependency are different from those of PKNalpha." BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, vol. 261, no. 3, 11 August 1999 (1999-08-11), pages 808-814, XP002165839 ISSN: 0006-291X figure 1 DOC. AGAINST INV. 9 (SEQ.IDs. 130, 12)	1-15,26, 27,35,37
X	DATABASE EMBL 'Online! Accession Number H19102, 2 July 1995 (1995-07-02) HILLIER L. ET AL.: "Homo sapiens cDNA clone IMAGE:171993 5' similar to SP:F31E3.2 CE01267 protein kinase." XP002165847 abstract DOC. AGAINST INV. 11 (SEQ.IDs. 132, 14)	2,6,7, 11,12
X	WO 97 33909 A (CORIXA CORP) 18 September 1997 (1997-09-18)  SEQ.IDs.6 and 16 DOC. AGAINST INV. 12 (SEQ.IDs. 133, 15)	2,6,7,9, 11,12, 26,27, 35-38
<b>X</b>	DATABASE EMBL 'Online! Accession Number AA463334, 13 June 1997 (1997-06-13) HILLIER L. ET AL.: "Homo sapiens cDNA clone IMAGE:811660 5' similar to SW:COT1_NEUCR P38679 serine/threonine-protein kinase COT-1."XP002165848 abstract	1,2,4,6, 7,10-13, 15
Ρ,Χ	DOC. AGAINST INV. 12 (SEQ.IDs. 133, 15)  WO 99 57144 A (INCYTE PHARMA INC; PATTERSON CHANDRA (US); AZIMZAI YALDA (US); RED) 11 November 1999 (1999-11-11)  SEQ.IDs. 52 and 117 DOC. AGAINST INV. 12 (SEQ.IDs. 133, 15)  -/	2,6,7,9, 11,12, 26,27, 29,30, 35-38

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

Int Jonal Application No PCT/US 00/14842

Category °	etion) DOCUMENTS CONSIDERED TO BE RELEVANT  Citation of document, with indication where appropriate, of the relevant passages	Relevant to claim No.
Ρ,Χ	ZHANG H. ET AL.: "Cloning, characterization, and chromosome mapping of RPS6KC1, a novel putative member of the ribosome protein S6 kinase family, to chromosome 12q12-q13.1." GENOMICS, vol. 61, no. 3, 1 November 1999 (1999-11-01), pages 314-318, XP002165840 ISSN: 0888-7543 the whole document DOC. AGAINST INV. 12 (SEQ.IDs. 133, 15)	1-15,35
X	DATABASE EMBL 'Online! Accession Number AC006530, 8 February 1999 (1999-02-08) ROWEN L. ET AL.: "Sequencing of human chromosome 14." XP002165849 abstract DOC. AGAINST INV. 14 (SEQ.IDs. 135, 17)	1,2,4-7, 10-15
X	DATABASE EMBL 'Online! Accession Number AI215680, 23 October 1998 (1998-10-23) STRAUSBERG R.: "Homo sapiens cDNA clone IMAGE:1884219." XP002165850 abstract DOC. AGAINST INV. 14 (SEQ.IDs. 135, 17)	6,7
x	WO 98 11234 A (HAWKINS PHILLIP R ;INCYTE PHARMA INC (US); AU YOUNG JANICE (US); G) 19 March 1998 (1998-03-19) SEQ.IDs. 5 and 6 DOC. AGAINST INV. 15 (SEQ.IDs. 136, 18) DOC. AGAINST INV. 16 (SEQ.IDs. 137, 19)	1-15, 26-30, 35-38
X	EP 0 861 896 A (DADE BEHRING MARBURG GMBH) 2 September 1998 (1998-09-02)  SEQ.IDs. 1 and 2  DOC. AGAINST INV. 15 (SEQ.IDs. 136, 18)  DOC. AGAINST INV. 16 (SEQ.IDs. 137, 19)	1-15, 26-28, 35-38
Ρ,Χ	DATABASE EMBL 'Online! Accession Number AF205855, 23 December 1999 (1999-12-23) SHIGAEV A. ET AL.: "Mus musculus serum and glucocorticoid-dependent protein kinase (Sgk) mRNA." XP002165851 abstract DOC. AGAINST INV. 16 (SEQ.IDs. 137, 19)	1,2,4,6, 7,10-13, 15

16

Form PCT/ISA/210 (continuation of second sneet) (July 1992)

Int cional Application No PCT/US 00/14842

ation) DOCUMENTS CONSIDERED TO BE RELEVANT  Citation of document, with indication where appropriate, of the relevant passages	Relevant to claim No.
Gastion of Columnia indication, many appropriate, of the felevant passages	rielevani io cialin ivo.
WO 00 35946 A (UNIV DUNDEE ;COHEN PHILIP (GB); DEAK MARIA (GB); KOBAYASHI TAKAYAS) 22 June 2000 (2000-06-22) figure 11 DOC. AGAINST INV. 17 (SEQ.IDs. 138, 20)	1-14,26, 27,29,30
DOC. AGAINST INV. 113 (SEQ.IDs. 234, 116)	
DATABASE EMBL 'Online! Accession Number Z98752, 23 August 1997 (1997-08-23) RAMSAY H.: "Human DNA sequence from clone RP1-13887 on chromosome 20q13.12." XP002165852 abstract DOC. AGAINST INV. 17 (SEQ.IDs. 138, 20)	1-14
WO 98 31802 A (GENETICS INST) 23 July 1998 (1998-07-23) SEQ.IDs. 13 and 14 DOC. AGAINST INV. 21 (SEQ.IDs. 142, 24)	6,7,11, 12
DATABASE EMBL 'Online! Accession Number AI061003, 23 July 1998 (1998-07-23) MARRA M. ET AL.: "Mus musculus cDNA clone IMAGE:1379597 5' similar to TR:008875 calcium calmodulin dependent kinase CPG16." XP002165853 abstract DOC AGAINST INV 22 (SEO IDs 143 25)	1,2,4,6, 7,10-13, 25
DATABASE EMBL 'Online! Accession Number AA383293, 18 April 1997 (1997-04-18) ADAMS M. D. ET AL.: "Homo sapiens cDNA 5'-end similar to serine/threonine kinase p78." XP002165854 abstract DOC. AGAINST INV. 23 (SEQ.IDs. 144, 26)	1,2,4,6, 7,10-13, 16
DATABASE EMBL 'Online! Accession number AA197883, 29 January 1997 (1997-01-29) MARRA M. ET AL.: "Mus musculus cDNA clone IMAGE:654045 5' similar to TR:G406113 protein kinase I." XP002165855 abstract DOC. AGAINST INV. 24 (SEQ.IDs. 145, 27)	1,2,4,6, 7,10-13
	(GB); DEAK MARIA (GB); KOBAYASHI TAKAYAS) 22 June 2000 (2000-06-22) figure 11 DOC. AGAINST INV. 17 (SEQ.IDS. 138, 20) DOC. AGAINST INV. 113 (SEQ.IDS. 234, 116)  DATABASE EMBL 'Online! Accession Number Z98752, 23 August 1997 (1997-08-23) RAMSAY H.: "Human DNA sequence from clone RP1-13887 on chromosome 20q13.12." XP002165852 abstract DOC. AGAINST INV. 17 (SEQ.IDS. 138, 20)  WO 98 31802 A (GENETICS INST) 23 July 1998 (1998-07-23) SEQ.IDS. 13 and 14 DOC. AGAINST INV. 21 (SEQ.IDS. 142, 24)  DATABASE EMBL 'Online! Accession Number AIO61003, 23 July 1998 (1998-07-23) MARRA M. ET AL.: "Mus musculus cDNA clone IMAGE:1379597 5' similar to TR:008875 calcium calmodulin dependent kinase CPG16." XP002165853 abstract DOC. AGAINST INV. 22 (SEQ.IDS. 143, 25)  DATABASE EMBL 'Online! Accession Number AA383293, 18 April 1997 (1997-04-18) ADAMS M. D. ET AL.: "Homo sapiens cDNA 5'-end similar to serine/threonine kinase p78." XP002165854 abstract DOC. AGAINST INV. 23 (SEQ.IDS. 144, 26)  DATABASE EMBL 'Online! Accession number AA197883, 29 January 1997 (1997-01-29) MARRA M. ET AL.: "Mus musculus cDNA clone IMAGE:654045 5' similar to TR:G406113 protein kinase I." XP002165855 abstract

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

Int .tional Application No PCT/US 00/14842

	of document, with indication, where appropriate, of the relevant passages	Polovant to stain At-
	Telephone of the rath passages	Relevant to claim No.
;MI (J) pa	99 50395 A (HELIX RESEARCH INST URAMATSU MASAAKI (JP); TOKUMITSU HIROSHI P) 7 October 1999 (1999-10-07) ge 41 -page 51 C. AGAINST INV. 24 (SEQ.IDs. 145, 27)	1-4,6-13
sei de: tr JOI vo 30 290 ISS	NJO H. ET AL: "DRAKS, novel rine/threonine kinases related to ath-associated protein kinase that igger apoptosis."  JRNAL OF BIOLOGICAL CHEMISTRY, 1. 273, no. 44, 0ctober 1998 (1998-10-30), pages 066-29071, XP002165841 SN: 0021-9258 igure 1 C. AGAINST INV. 26 (SEQ.IDs. 147, 29)	1-14,16, 35,37
SEC DOC SEC	99 33961 A (AKIRA SHIZUO ; KAWAI TARO P); ASAHI CHEMICAL IND (JP)) July 1999 (1999-07-08) Q.IDs. 5 and 6 C. AGAINST INV. 26 (SEQ.IDs. 147, 29) Q.IDs. 29 and 30 C. AGAINST INV. 40 (SEQ.IDs. 161, 43)	1-14,16, 26,27, 29,30, 35,37
COI GEN NEW LAF DN/ vo pag ISS the -& ACO 9 / NAO KI/ XPO abs NAO KI/ XPO abs	GASE T. ET AL.: "PREDICTION OF THE DING SEQUENCE OF UNIDENTIFIED HUMAN NES. XIII. THE COMPLETE SEQUENCE OF 100 N CDNA CLONES FROM BRAIN WHICH CODE FOR RGE PROTEINS IN VITRO" A RESEARCH, I. 6, 26 February 1999 (1999-02-26), ges 63-70, XP000952912 SN: 1340-2838 E whole document DATABASE EMBL 'Online! Cession Number AB023153, April 1999 (1999-04-09) GASE T. ET AL.: "Homo sapiens mRNA for AA0936 protein." D02166242 Stract C. AGAINST INV. 54 (SEQ.IDs. 175, 57) DATABASE EMBL 'Online! Cession Number AB023216, April 1999 (1999-04-09) GASE T. ET AL.: "Homo sapiens mRNA for AA0999 protein." D02166243 Stract C. AGAINST INV. 28 (SEQ.IDs. 149, 31)	1,2,4-7, 10-14, 16,19

16

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

Int .tionel Application No PCT/US 00/14842

(	WO 98 01756 A (UNIV WASHINGTON) 15 January 1998 (1998-01-15) SEQ.IDs. 1 and 2 DOC. AGAINST INV. 30 (SEQ.IDs. 151, 33) DATABASE EMBL 'Online!	1-14,16, 26,27, 35,36
(	15 January 1998 (1998-01-15)  SEQ.IDs. 1 and 2  DOC. AGAINST INV. 30 (SEQ.IDs. 151, 33)	26,27,
	DOC. AGAINST INV. 30 (SEQ.IDs. 151, 33)	
	DATABASE EMBL 'Online!	
	Accession Number W90839, 9 July 1996 (1996-07-09) MARRA M. ET AL.: "Mus musculus cDNA clone IMAGE: 420441 5' similar to gb: M80359 putative serine/threonine protein kinase."	1,2,4,6, 7,10-13, 16
	XPO02165856 abstract DOC. AGAINST INV. 31 (SEQ.IDs. 152, 34)	
	NAGASE T. ET AL.: "PREDICTION OF THE CODING SEQUENCES OF UNIDENTIFIED HUMAN GENES. IV. THE CODING SEQUENCES OF 40 NEW GENES (KIAAO121-KIAAO160) DEDUCED BY ANALYSIS OF CDNA CLONES FROM HUMAN CELL	1,2,4-7, 10-14,16
	LINE KG-1" DNA RESEARCH, vol. 2, no. 4, 31 August 1995 (1995-08-31), pages 167-174, XP000676653 ISSN: 1340-2838 the whole document -& DATABASE EMBL 'Online! Accession Number D50925, 1 August 1996 (1996-08-01)	
	NAGASE T. ET AL.: "Human mRNA for KIAA0135 gene." XP002166244 abstract DOC. AGAINST INV. 32 (SEQ.IDs. 153, 35) DOC. AGAINST INV. 33 (SEQ.IDs. 154, 36)	
<b>(</b>	DATABASE _EMBL 'Online!_ Accession Number U79240, 14 December 1996 (1996-12-14) YU W. ET AL.: "Human serine/threonine kinase mRNA." XP002165857 abstract DOC. AGAINST INV. 33 (SEQ.IDs. 154, 36)	1,2,4-7, 10-14
	-/	
-		-

Form PCT/ISA/210 (continuation of second sneet) (July 1992)

Int cional Application No PCT/US 00/14842

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT  Category * Citation of document, with indication where appropriate of the relevant passages.		
Jalegory °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EMBL 'Online! Accession Number AI036899, 29 June 1998 (1998-06-29) MARRA M. ET AL.: "Mus musculus cDNA clone IMAGE:1746011 5' similar to TR:Q99763 serine/threonine protein kinase." XP002165858 abstract DOC. AGAINST INV. 33 (SEQ.IDs. 154, 36)	1,2,4,6, 7,10-13
X	DATABASE EMBL 'Online! Accession Number AI469033, 17 March 1999 (1999-03-17) STRAUSBERG R.: "Homo sapiens cDNA clone IMAGE:2137322." XP002165859 abstract DOC. AGAINST INV. 35 (SEQ.IDs. 156, 38)	6,7
X	DATABASE EMBL 'Online! Accession Number AC007225, 7 April 1999 (1999-04-07) BRUCE D. ET AL.: "Homo sapiens chromosome 16 clone RPCI-11_480G7." XP002166245 abstract DOC. AGAINST INV. 37 (SEQ.IDs. 158, 40)	6,7
Ρ,Χ	WO 99 49062 A (FAN WUFANG ;GENE LOGIC INC (US); PRASHAR YATINDRA (US)) 30 September 1999 (1999-09-30) SEQ.IDs. 1 and 2 DOC. AGAINST INV. 37 (SEQ.IDs. 158, 40) DOC. AGAINST INV. 55 (SEQ.IDs. 176, 58)	1-14, 26-30, 35-38
X	DATABASE EMBL 'Online! Accession Number AI596766, 26 April 1999 (1999-04-26) MARRA M. ET AL.: "Mus musculus cDNA clone IMAGE:949322 5' similar to WP:ZC373.4 CE02377 myosin-light-chain kinase domain." XP002166246 abstract DOC. AGAINST INV. 38 (SEQ.IDs. 159, 41) DOC. AGAINST INV. 39 (SEQ.IDs. 160, 42) -/	1,2,4,6, 7,10-13, 16

16

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

tnt. donal Application No
PCT/US 00/14842

	continuation) DOCUMENTS CONSIDERED TO BE RELEVANT  CORP. Citation of document, with indication where appropriate of the relevant passages.  Relevant to claim No.		
legory *	Chation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	
, X	NAGASE T. ET AL.: "PREDICTION OF THE CODING SEQUENCES OF UNIDENTIFIED HUMAN GENES. XVI. THE COMPLETE SEQUENCES OF 150 NEW CDNA CLONES FROM BRAIN WHICH CODE FOR LARGE PROTEINS IN VITRO" DNA RESEARCH, vol. 7, 28 February 2000 (2000-02-28), pages 65-73, XP000923011 KIAA1297 -& DATABASE EMBL 'Online! Accession Number AB037718, 14 March 2000 (2000-03-14) OHARA O. ET AL.: "Homo sapiens mRNA for KIAA1297 protein." XP002166247 abstract DOC. AGAINST INV. 38 (SEQ.IDs. 159, 41) DOC. AGAINST INV. 39 (SEQ.IDs. 160, 42) -& DATABASE EMBL 'Online! Accession Number AB037759, 14 March 2000 (2000-03-14) OHARA O. ET AL.: "Homo sapiens mRNA for KIAA1338 protein." XP002167889 abstract	1,2,4-7, 10-14, 16,25	
	DOC. AGAINST INV. 67 (SEQ.IDs. 188, 70) -& DATABASE EMBL 'Online! Accession Number AB037790, 14 March 2000 (2000-03-14) OHARA O. ET AL.: "Homo sapiens mRNA for KIAA1369 protein." XP002167890 abstract DOC. AGAINST INV. 68 (SEQ.IDs. 189, 71) -& DATABASE EMBL 'Online! Accession Number AB037781, 14 March 2000 (2000-03-14) NAGASE T. ET AL.: "Homo sapiens mRNA for KIAA1360 protein, partial cds." XP002168226		
	abstract DOC. AGAINST INV. 82 (SEQ.IDs. 203, 85)		
x	KAWAI T. ET AL.: "Duet is a novel serine/threonine kinase with Dbl-Homology (DH) and Pleckstrin-Homology (PH) domains" GENE, vol. 227, no. 2, 18 February 1999 (1999-02-18), pages 249-255, XP004158739 ISSN: 0378-1119 the whole document DOC. AGAINST INV. 40 (SEQ.IDs. 161, 43)	1-14,29, 30,35-38	

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

Int .tional Application No
PCT/US 00/14842

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT			
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	
X	DATABASE EMBL 'Online! Accession Number AA454060, 11 June 1997 (1997-06-11) HILLIER L. ET AL.: "Homo sapiens cDNA clone IMAGE:795492 5' similar to TR:G49075 calmodulin-binding protein." XP002166248 abstract DOC. AGAINST INV. 41 (SEQ.IDs. 162, 44)	6,7	
X	DATABASE EMBL 'Online! Accession Number AI385971, 29 January 1999 (1999-01-29) MARRA M. ET AL.: "Mus musculus cDNA clone IMAGE:514336 5' similar to WP:R90.1 CE06325 protein kinase." XP002166249 abstract DOC. AGAINST INV. 43 (SEQ.IDs. 164, 46)	1,2,4,6, 7,10-13, 16	
X	DATABASE EMBL 'Online! Accession Number AA436054, 1 June 1997 (1997-06-01) HILLIER L. ET AL.: "Homo sapiens cDNA clone IMAGE:730582 5' similar to gb:X66363 serine/threonine-protein kinase pctaire-1" XP002166250 abstract DOC. AGAINST INV. 44 (SEQ.IDs. 165, 47)	1,2,4-7, 10-14,16	
X	DATABASE EMBL 'Online! Accession Number AA061797, 24 September 1996 (1996-09-24) MARRA M. ET AL.: "Mus musculus cDNA clone IMAGE:513953 5' similar to gb:X66358 serine/threonine-protein kinase." XP002166251 abstract DOC. AGAINST INV. 45 (SEQ.IDs. 166, 48) DOC. AGAINST INV. 46 (SEQ.IDs. 167, 49)	1,2,4,6, 7,10-13, 17	
A	WO 98 35015 A (GERHOLD DAVID L ; MERCK & CO INC (US)) 13 August 1998 (1998-08-13) SEQ.IDs.2 and 3 DOC. AGAINST INV. 50 (SEQ.IDs. 171, 53) DOC. AGAINST INV. 114 (SEQ.IDs. 235, 117)	1-30, 35-38	

Form PCT/ISA/210 (continuation of second sneet) (July 1992)

Int dional Application No PCT/US 00/14842

Relevant to claim No.
newall to claim No.
1-4, 6-13,18, 26,27
1-14,18, 26-30, 35-38
1,2,4,6, 7,10-13, 18
1,2,4-7, 10-14,18
2,6,7,

Form PCT/ISA/210 (continuation of second sneet) (July 1992)

Int. ional Application No PCT/US 00/14842

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT  Category Citation of document, with indication, where appropriate, of the relevant passages  Relevant to claim No.		Relevant to claim No.
X	NAGASE T. ET AL.: "Prediction of the coding sequences of unidentified human genes. VII. The complete sequences of 100 new cDNA clones from brain which can code for large proteins in vitro" DNA RESEARCH, vol. 4, no. 4, 28 April 1997 (1997-04-28), pages 141-150, XP002102085 ISSN: 1340-2838 the whole document -& DATABASE EMBL 'Online! Accession Number AB002342, 1 July 1997 (1997-07-01) NAGASE T. ET AL.: "Human mRNA for KIAA0344 gene." XP002167894 abstract DOC. AGAINST INV. 59 (SEQ.IDs. 180, 62)	2,6,7, 11,12
<b>(</b>	WO 98 36054 A (HOOPER JOHN DAVID ; AMRAD OPERATIONS PTY LTD (AU); ANTALIS TONI MAR) 20 August 1998 (1998-08-20) SEQ.IDs. 9 and 10 DOC. AGAINST INV. 60 (SEQ.IDs. 181, 63)	1-14, 26-30, 35-38
X	ANDERSON K. A. ET AL.: "Components of a calmodulin-dependent protein kinase cascade. Molecular cloning, functional characterization and cellular localization of Ca2+/calmodulin-dependent protein kinase kinase beta."  JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 273, no. 48, 27 November 1998 (1998-11-27), pages 31880-31889, XP002167887  ISSN: 0021-9258 the whole document  -& DATABASE EMBL 'Online! Accession Number AF140507, 21 May 1999 (1999-05-21) ANDERSON K. A. ET AL.: "Homo sapiens Ca2+/calmodulin-dependent protein kinase beta, complete cds." XP002167895 abstract DOC. AGAINST INV. 62 (SEQ.IDs. 183, 65)	1-14,23, 26,27
Ρ,Χ	WO 99 58558 A (INCYTE PHARMA INC; PATTERSON CHANDRA (US); YUE HENRY (US); BANDMAN) 18 November 1999 (1999-11-18) SEQ.IDs. 2 and 15 DOC. AGAINST INV. 62 (SEQ.IDs. 183, 65)	2,6,7,9, 11,12, 26-28

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

Int Jonal Application No PCT/US 00/14842

	tion) DOCUMENTS CONSIDERED TO BE RELEVANT	Polyupat to plains his
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EMBL 'Online! Accession Number AC004685, 15 May 1998 (1998-05-15) ADAMS M. D. AND LOFTUS B. J.: "Homo sapiens chromosome 16 BAC clone CIT987SK-A-233A8." XP002167896 abstract DOC. AGAINST INV. 63 (SEQ.IDs. 184, 66)	1,2,4-7
Ρ,Χ	US 6 013 455 A (AZIMZAI YALDA ET AL) 11 January 2000 (2000-01-11) SEQ.IDs. 2 and 11	1-14, 26-30, 35-38
	DOC. AGAINST INV. 63 (SEQ.IDs. 184, 66)	
X	EP 0 870 825 A (SMITHKLINE BEECHAM CORP) 14 October 1998 (1998-10-14)	1-14, 25-30, 35-38
	figure 2 DOC. AGAINST INV. 65 (SEQ.IDs. 186, 68) DOC. AGAINST INV. 66 (SEQ.IDs. 187, 69)	
<b>X</b>	DATABASE EMBL 'Online! Accession Number AA589241, 18 September 1997 (1997-09-18) MARRA M. ET AL.: "Mus musculus cDNA clone IMAGE:992145 5' similar to WP:F49E11.1 CE05897 serine/threonine protein kinase." XP002167897 abstract DOC. AGAINST INV. 66 (SEQ.IDs. 187, 69)	1,2,4,6, 7,10-13, 25
Ρ,Χ	BERLANGA J. J. ET AL.: "Characterization of a mammalian homolog of the GCN2 eukaryotic initiation factor 2alpha kinase."  EUROPEAN JOURNAL OF BIOCHEMISTRY, vol. 265, no. 2, October 1999 (1999-10), pages 754-762, XP002167888 ISSN: 0014-2956 the whole document DOC. AGAINST INV. 67 (SEQ.IDs. 188, 70)	1-14, 25-27,35
X	WO 94 05794 A (MASSACHUSETTS INST TECHNOLOGY) 17 March 1994 (1994-03-17) page 13, paragraph 2 examples 1,2 DOC. AGAINST INV. 68 (SEQ.IDs. 189, 71)	1-14, 26-28, 35-38

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

Int. .ional Application No PCT/US 00/14842

Category °	ation) DOCUMENTS CONSIDERED TO BE RELEVANT  Citation of document, with indication, where appropriate, of the relevant passages	
Calegory	Challott of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MELLOR H. ET AL.: "CLONING AND CHARACTERIZATION OF CDNA ENCODING RAT HEMIN-SENSITIVE INITIATION FACTOR-2ALPHA (EIF-2ALPHA) KINASE" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 269, no. 14, 8 April 1994 (1994-04-08), pages 10201-10204, XP002920790 ISSN: 0021-9258 the whole document DOC. AGAINST INV. 68 (SEQ.IDs. 189, 71)	1-4,6-13
X	DATABASE EMBL 'Online! Accession Number AA387681, 25 June 1997 (1997-06-25) MARRA M. ET AL.: "Mus musculus cDNA clone." XP002167898 abstract DOC. AGAINST INV. 70 (SEQ.IDs. 191, 73)	6,7
P,X	W0 00 09678 A (TULARIK INC) 24 February 2000 (2000-02-24)  the whole document	1-14,20, 26,27, 29,30, 35-38
X	DOC. AGAINST INV. 71 (SEQ.IDs. 192, 74)  DATABASE EMBL 'Online! Accession Number AF046653,	1-4, 6-13,25
	6 April 1998 (1998-04-06) ZAMBROWICZ B. P. ET AL.: "Mus musculus genomic clone OST10140." XP002167969 abstract DOC. AGAINST INV. 76 (SEQ.IDs. 197, 79)	
Ρ,Χ	DATABASE EMBL 'Online! Accession Number AF238255, 12 April 2000 (2000-04-12) LIU T. C. ET AL.: "Homo sapiens mixed lineage kinase mRNA." XP002167970 abstract -& LIU TC. ET AL.: "Cloning and expression of ZAK, a mixed lineage kinase-like protein containing a leucine-zipper and a sterile-alpha motif." BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, vol. 274, 11 August 2000 (2000-08-11), pages 811-816, XP002167968 the whole document DOC. AGAINST INV. 77 (SEQ.IDs. 198, 80)	1-14
	-/	

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

Int. :ional Application No PCT/US 00/14842

C.(Continu	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 00 14212 A (ACTON SUSAN ;MILLENNIUM PHARM INC (US)) 16 March 2000 (2000-03-16)	1-14, 25-30, 35-38
	figure 2 DOC. AGAINST INV. 77 (SEQ.IDs. 198, 80) figure 3 DOC. AGAINST INV. 106 (SEQ.IDs. 227, 109)	
х	DATABASE EMBL 'Online! Accession Number AA270784, 28 March 1997 (1997-03-28) MARRA M. ET AL.: "Mus musculus cDNA clone IMAGE:736476." XP002167971 abstract DOC. AGAINST INV. 80 (SEQ.IDs. 201, 83)	6,7
Ρ,Χ	PAZDERNIK N. J. ET AL.: "MOUSE RECEPTOR INTERACTING PROTEIN 3 DOES NOT CONTAIN A CASPASE-RECRUITING OR A DEATH DOMAIN BUT INDUCES APOPTOSIS AND ACTIVATES NF-(KAPPA)B" MOLECULAR AND CELLULAR BIOLOGY, vol. 19, no. 10, October 1999 (1999-10), pages 6500-6508, XP000939146 the whole document DOC. AGAINST INV. 80 (SEQ.IDs. 201, 83)	1-4, 6-13,22
X	DATABASE EMBL 'Online! Accession Number AL031297, 13 August 1998 (1998-08-13) COBLEY V.: "Human DNA sequence from clone 97P20 on chromosome1q23.2-24.3." XP002168227 abstract DOC. AGAINST INV. 81 (SEQ.IDs. 202, 84)	1-14
<b>X</b> –	WO 99 04265 A (SAHIN UGUR ;TURECI OZLEM (DE); PFREUNDSCHUH-MICHAEL-(DE); GOUT IVA) - 28 January 1999 (1999-01-28) SEQ.IDs. 431 and 435 DOC. AGAINST INV. 82 (SEQ.IDs. 203, 85)	2,6,7,
X	DATABASE EMBL 'Online! Accession Number AA195964, 28 January 1997 (1997-01-28) HILLIER L. ET AL.: "Homo sapiens cDNA clone IMAGE:628136" XP002168228 abstract DOC. AGAINST INV. 84 (SEQ.IDs. 205, 87)	6,7
-	abstract	

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

Int. .ional Application No PCT/US 00/14842

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT  Category ° Citation of document, with indication, where appropriate, of the relevant passages  Relevant to citation of document, with indication, where appropriate is a citation of the relevant passages.		
on the relevant passages	Relevant to claim No.	
DATABASE EMBL 'Online! Accession Number AK000342, 22 February 2000 (2000-02-22) SUGANO S. ET AL.: "Homo sapiens cDNA FLJ20335 fis, clone HEP11429." XP002168229 abstract DOC. AGAINST INV. 84 (SEQ.IDs. 205, 87)	1-14	
DATABASE EMBL 'Online! Accession Number AF027406, 6 January 1999 (1999-01-06) BRENNER V. ET AL.: "Homo sapiens muscle-specific serine kinase 1 (MSSK1) mRNA." XP002168230 abstract DOC. AGAINST INV. 85 (SEQ.IDs. 206, 88)	1-14	
DATABASE EMBL 'Online! Accession Number AF043288, 6 January 1999 (1999-01-06) BRENNER V. ET AL.: "Mus musculus muscle-specific serine kinase 1 mRNA." XP002168231 abstract DOC. AGAINST INV. 85 (SEQ.IDs. 206, 88)	1-4,6-13	
WO OO 22143 A (INCYTE PHARMA INC ;AZIMZAI YALDA (US); CORLEY NEIL C (US); YUE HEN) 20 April 2000 (2000-04-20) SEQ.IDs. 1 and 10 DOC. AGAINST INV. 85 (SEQ.IDs. 206, 88) SEQ.IDs. 7 and 16 DOC. AGAINST INV. 104 (SEQ.IDs. 225, 107)	1-4, 6-13, 26-28	
DATABASE EMBL 'Online! Accession Number AI553938, 25 March 1999 (1999-03-25) STAUSBERG R.: "Homo sapiens cDNA clone IMAGE:2090493 3' similar to TR:015367 TSK_1." XP002168388 abstract DOC. AGAINST INV. 86 (SEQ.IDs. 207, 89) DOC. AGAINST INV. 87 (SEQ.IDs. 208, 90) DOC. AGAINST INV. 91 (SEQ.IDs. 212, 94)	1,2,4-7, 10-14,25	
	DATABASE EMBL 'Online! Accession Number AKO00342, 22 February 2000 (2000-02-22) SUGANO S. ET AL.: "Homo sapiens cDNA FLJ20335 fis, clone HEP11429." XP002168229 abstract DOC. AGAINST INV. 84 (SEQ.IDs. 205, 87)  DATABASE EMBL 'Online! Accession Number AF027406, 6 January 1999 (1999-01-06) BRENNER V. ET AL.: "Homo sapiens muscle-specific serine kinase 1 (MSSK1) mRNA." XP002168230 abstract DOC. AGAINST INV. 85 (SEQ.IDs. 206, 88)  DATABASE EMBL 'Online! Accession Number AF043288, 6 January 1999 (1999-01-06) BRENNER V. ET AL.: "Mus musculus muscle-specific serine kinase 1 mRNA." XP002168231 abstract DOC. AGAINST INV. 85 (SEQ.IDs. 206, 88)  WO 00 22143 A (INCYTE PHARMA INC ;AZIMZAI YALDA (US); CORLEY NEIL C (US); YUE HEN) 20 April 2000 (2000-04-20) SEQ.IDs. 1 and 10 DOC. AGAINST INV. 85 (SEQ.IDs. 206, 88) SEQ.IDs. 7 and 16 DOC. AGAINST INV. 104 (SEQ.IDs. 225, 107)  DATABASE EMBL 'Online! Accession Number AI553938, 25 March 1999 (1999-03-25) STAUSBERG R:: "Homo sapiens cDNA clone IMAGE:2090493 3' similar to TR:015367 TSK_1." XP002168388 abstract DOC. AGAINST INV. 86 (SEQ.IDs. 207, 89) DOC. AGAINST INV. 87 (SEQ.IDs. 208, 90)	

16

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

Into ional Application No
PCT/US 00/14842

(Continu	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	-,-
ategory °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	DATABASE EMBL 'Online! Accession Number AV040939, 14 May 1999 (1999-05-14) CARNINCI P. ET AL.: "Mus musculus adult male testis cDNA, partial sequence." XP002168389 abstract DOC. AGAINST INV. 87 (SEQ.IDs. 208, 90)	6,7
X	DATABASE EMBL 'Online! Accession Number AA399596, 29 April 1997 (1997-04-29) HILLIER L. ET AL.: "Homo sapiens cDNA clone IMAGE:729913 5' similar to TR:G404634 Serine/threonine kinase." XP002168766 abstract DOC. AGAINST INV. 88 (SEQ.IDs. 209, 91)	1,2,4-7, 10-14,25
X	KUENG P. ET AL: "A novel family of serine/threonine kinases participating in spermiogenesis."  JOURNAL OF CELL BIOLOGY, vol. 139, no. 7, 29 December 1997 (1997-12-29), pages 1851-1859, XP002168387 ISSN: 0021-9525 the whole document DOC. AGAINST INV. 89 (SEQ.IDs. 210, 92)	1-14, 26-28, 35-38
<b>x</b>	DATABASE EMBL 'Online! Accession Number AI652441, 5 May 1999 (1999-05-05) STRAUSBERG R.: "Homo sapiens cDNA clone IMAGE:2307063 3' similar to TR:P97417 serine/threonine kinase" XP002168390 abstract DOC. AGAINST INV. 89 (SEQ.IDs. 210, 92)	1,2,4-7, 10-14
X	DATABASE EMBL 'Online! Accession Number L77564, 16 June 1996 (1996-06-16) GONG W. ET AL.: "Homo sapiens DGS-G mRNA, 3'-end." XP002168391 abstract DOC. AGAINST INV. 89 (SEQ.IDs. 210, 92) -/	1,2,4-7, 10-14

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

Int. ional Application No
PCT/US 00/14842

	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to clarm No.
X	DATABASE EMBL 'Online! Accession NumberAA905446, 9 April 1998 (1998-04-09) STRAUSBERG R.: "Homo sapiens cDNA clone IMAGE:1506197 3' similar to TR:P97417 serine threonine kinase." XP002168767 abstract DOC. AGAINST INV. 91 (SEQ.IDs. 212, 9) DOC. AGAINST INV. 86 (SEQ.IDs. 207, 89)	1,2,4-7, 10-14,25
X	DATABASE EMBL 'Online! Accession Number AI538521, 24 March 1999 (1999-03-24) STRAUSBERG R.: "Homo sapiens cDNA clone IMAGE:2074994 3' similar to SW:UN51_CAEEL Q23023 serine/threonine protein kinase UNC-51" XP002168768 abstract DOC. AGAINST INV. 92 (SEQ.IDs. 213, 95) DOC. AGAINST INV. 93 (SEQ.IDs. 214, 96)	1,2,4-7, 10-14,25
X	DATABASE EMBL 'Online! Accession Number AA498104, 3 July 1997 (1997-07-03) MARRA M. ET AL.: "Mus musculus cDNA clone IMAGE:918101." XP002168769 abstract DOC. AGAINST INV. 93 (SEQ.IDs. 214, 96)	6,7
X	DATABASE EMBL 'Online! Accession Number AA215311, 5 February 1997 (1997-02-05) STRAUSBERG R.: "Homo sapiens cDNA clone IMAGE:63368 5' similar to TR:E237261 calmodulin-domain protein kinase." XP002168770 abstract DOC. AGAINST INV. 94 (SEQ.IDs. 215, 97)	1,2,4-7, 10-14
Ρ,Χ	WO 99 32609 A (KAROLINSKA INNOVATIONS AB; ZAPHIROPOULOS PETER G (SE); TOFTGAARD R) 1 July 1999 (1999-07-01) SEQ.IDs. 1 and 2 DOC. AGAINST INV. 95 (SEQ.IDs. 216, 98)	1-14,18, 26-28, 35-38

16

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

Int. Ional Application No PCT/US 00/14842

	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EMBL 'Online! Accession Number AA018361, 10 August 1996 (1996-08-10) HILLIER L. ET AL.: "Homo sapiens cDNA clone IMAGE:361543 5' similar to SW:ASK1_ARATH P43291 serine/threonine kinase ASK2." XP002169144 abstract DOC. AGAINST INV. 95 (SEQ.IDs. 216, 98)	1,2,4-7, 10-14,18
x	DATABASE EMBL 'Online! Accession Number AI651075, 5 May 1999 (1999-05-05) STRAUSBERG R.: "Homo sapines cDNA clone IMAGE:2304078 3' similar to TR:060679 serum inducible kinase." XP002169145 abstract DOC. AGAINST INV. 97 (SEQ.IDs. 218, 100)	1,2,4-7, 10-14,25
X	DATABASE EMBL 'Online! Accession Number W08549, 27 April 1996 (1996-04-27) MARRA M. ET AL.: "Mus musculus cDNA clone IMAGE:332593." XP002169146 abstract DOC. AGAINST INV. 98 (SEQ.IDs. 219, 101)	6,7
x	DATABASE EMBL 'Online! Accession Number AC002355, 24 July 1997 (1997-07-24) HAWKINS T. L. ET AL.: "Homo sapiens chromosome 9 clone 107G20 map 9q34" XP002169147 abstract DOC. AGAINST INV. 99 (SEQ.IDs. 220, 102)	1-7
X	DATABASE EMBL 'Online! Accession Number AI606679, 26 April 1999 (1999-04-26) MARRA M. ET AL.: "Mus musculus cDNA clone IMAGE:516008." XP002169148 abstract DOC. AGAINST INV.100 (SEQ.IDs. 221, 103)	6,7
1		-

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

Int: Jonal Application No
PCT/US 00/14842

ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
DATABASE EMBL 'Online! Accession Number AA493011, 2 July 1997 (1997-07-02) MARRA. M. ET AL.: "Mus musculus cDNA clone IMAGE:917574." XP002169149 abstract DOC. AGAINST INV.100 (SEQ.IDs. 221, 103)	6,7
DATABASE EMBL 'Online! Accession Number AA396601, 28 April 1997 (1997-04-28) MARRA M. ET AL.: "Mus musculus cDNA clone IMAGE:570118." XP002169150 abstract DOC. AGAINST INV.102 (SEQ.IDs. 223, 105)	6,7
EP 1 033 401 A (GENSET SA) 6 September 2000 (2000-09-06) SEQ.ID.6560 DOC. AGAINST INV.102 (SEQ.IDs. 223, 105)	2,6,7, 11,12
DATABASE EMBL 'Online! Accession Number AA276191, 3 April 1997 (1997-04-03) MARRA M. ET AL.: " Mus musculus cDNA clone IMAGE:776192 5' similar t SW:KRB1_VACCC P20505 30 KD prtein kinase homolog." XP002169151 abstract DOC. AGAINST INV.104 (SEQ.IDs. 225, 107)	1-4,6-13
DATABASE EMBL 'Online! Accession Number AA399022, 29 April 1997 (1997-04-29) HILLIER L. ET AL.: "Homo sapiens cDNA clone IMAGE:729929." XP002169312 abstract DOC. AGAINST INV.106 (SEQ.IDs. 227, 109)	6,7
WO 97 47750 A (IMMUNEX CORP) 18 December 1997 (1997-12-18)  the whole document DOC. AGAINST INV.108 (SEQ.IDs. 229, 111)	1-14, 25-30, 35-38
	DATABASE EMBL 'Online! Accession Number AA493011, 2 July 1997 (1997-07-02) MARRA. M. ET AL.: "Mus musculus cDNA clone IMAGE:917574." XP002169149 abstract DOC. AGAINST INV.100 (SEQ.IDs. 221, 103)  DATABASE EMBL 'Online! Accession Number AA396601, 28 April 1997 (1997-04-28) MARRA ET AL.: "Mus musculus cDNA clone IMAGE:570118." XP002169150 abstract DOC. AGAINST INV.102 (SEQ.IDs. 223, 105)  EP 1 033 401 A (GENSET SA) 6 September 2000 (2000-09-06) SEQ.ID.6560 DOC. AGAINST INV.102 (SEQ.IDs. 223, 105)  DATABASE EMBL 'Online! Accession Number AA276191, 3 April 1997 (1997-04-03) MARRA M. ET AL.: "Mus musculus cDNA clone IMAGE:776192 5' similar t SW:KRB1_VACCC P20505 30 KD prtein kinase homolog." XP002169151 abstract DOC. AGAINST INV.104 (SEQ.IDs. 225, 107)  DATABASE EMBL 'Online! Accession Number AA399022, 29 April 1997 (1997-04-29) HILLIER L. ET AL.: "Homo sapiens cDNA clone IMAGE:729929." XP002169312 abstract DOC. AGAINST INV.106 (SEQ.IDs. 227, 109) WO 97 47750 A (IMMUNEX CORP) 18 December 1997 (1997-12-18) the whole document DOC. AGAINST INV.108 (SEQ.IDs. 229, 111)

16

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

Int. .ional Application No PCT/US 00/14842

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT  Category Citation of document, with indication, where appropriate, of the relevant passages  Relevant to claim No.		
	DATABASE EMBL 'Online! Accession Number AI298668, 4 December 1998 (1998-12-04) STRAUSBERG R.: "Homo sapiens cDNA clone IMAGE:1895716 3' similar to SW:NEK1_Mouse P51945 serine/threonine-protien kinase NEK1." XP002169313 abstract DOC. AGAINST INV.108 (SEQ.IDs. 229, 111)	1,2,4-7, 10-14,25
(	WANG X. S. ET AL.: "MAPKKK6, a novel mitogen-activated protein kinase kinase kinase kinase, that associates with MAPKKK5." BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, vol. 253, no. 1, 9 December 1998 (1998-12-09), pages 33-37, XP002169311 ISSN: 0006-291X the whole document DOC. AGAINST INV.109 (SEQ.IDs. 230, 112)	1-14,25
X	DATABASE EMBL 'Online! Accession Number AI638161, 29 April 1999 (1999-04-29) STRAUSBERG R.: "Homo sapiens cDNA cloneIMAGE:2239185 3' similar to SW:PAK3_Human 075914 serine/threonine-protein kinase." XP002169314 abstract DOC. AGAINST INV.110 (SEQ.IDs. 231, 113)	1,2,4-7, 10-14
P,X	NAGASE T. ET AL.: "PREDICTION OF THE CODING SEQUENCES OF UNIDENTIFIED HUMAN GENES. XV. THE COMPLETE SEQUENCES OF 100 NEW CDNA CLONES FROM BRAIN WHICH CODE FOR LARGE PROTEINS IN VITRO"	1-14
	DNA RESEARCH, vol. 6, 29 October 1999 (1999-10-29), pages 337-345, XP000865804 ISSN: 1340-2838 -& DATABASE EMBL 'Online! Accession Number AB033090,	
	11 November 1999 (1999-11-11) OHARA O. ET AL.: "Homo sapiens mRNA for KIAA1264 protein." XP002169637 abstract DOC. AGAINST INV.110 (SEQ.IDs. 231, 113)	
	1 ,,	

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

Int. ional Application No
PCT/US 00/14842

ation) DOCUMENTS CONSIDERED TO BE RELEVANT	PCT/US 00/14842
Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
DATABASE EMBL 'Online! Accession Number H29272, 19 July 1995 (1995-07-19) HILLIER L. ET AL.: "Homo sapiens cDNA clone IMAGE:49948." XP002169315 abstract DOC. AGAINST INV.111 (SEQ.IDs. 232, 114)	6,7
WO 99 64589 A (ZENECA LTD) 16 December 1999 (1999-12-16)  the whole document DOC. AGAINST INV.111 (SEQ.IDs. 232, 114) DOC. AGAINST INV.112 (SEQ.IDs. 233, 115)	1-14,23, 26-30, 35-38
DATABASE EMBL 'Online! Accession Number AA098024, 27 October 1996 (1996-10-27) MARRA M. ET AL.: "Mus musculus cDNA clone IMAGE:550913 5' similar to SW:DROME P18475 tyrosine-protein kinase receptor torso precursor." XP002169442 abstract DOC. AGAINST INV.112 (SEQ.IDs. 233, 115)	1-4, 6-13,23
DATABASE EMBL 'Online! Accession Number Z98752, 23 August 1997 (1997-08-23) RAMSAY H.: "Human DNA sequence from clone RP1-138B7 on chromosome 20q13.12." XP002169443 nts. 43893 - 62413 DOC. AGAINST INV.113 (SEQ.IDs. 234, 116)	1-14
DATABASE EMBL 'Online! Accession Number AF035013, 4 January 1999 (1999-01-04) JIANG Y. AND ZHAO K.: "Homo sapiens cell cycle related kinase mRNA, complete cds." XP002169444 abstract DOC. AGAINST INV.114 (SEQ.IDs. 235, 117)	1-14,24
	DATABASE EMBL 'Online! Accession Number H29272, 19 July 1995 (1995-07-19) HILLIER L. ET AL.: "Homo sapiens cDNA clone IMAGE:49948." XP002169315 abstract DOC. AGAINST INV.111 (SEQ.IDs. 232, 114) W0 99 64589 A (ZENECA LTD) 16 December 1999 (1999-12-16)  the whole document DOC. AGAINST INV.111 (SEQ.IDs. 232, 114) DOC. AGAINST INV.112 (SEQ.IDs. 233, 115)  DATABASE EMBL 'Online! Accession Number AA098024, 27 October 1996 (1996-10-27) MARRA M. ET AL.: "Mus musculus cDNA clone IMAGE:550913 5' similar to SW:DROME P18475 tyrosine-protein kinase receptor torso precursor." XP002169442 abstract DOC. AGAINST INV.112 (SEQ.IDs. 233, 115)  DATABASE EMBL 'Online! Accession Number Z98752, 23 August 1997 (1997-08-23) RAMSAY H.: "Human DNA sequence from clone RP1-138B7 on chromosome 20q13.12." XP002169443 nts. 43893 - 62413 DOC. AGAINST INV.113 (SEQ.IDs. 234, 116)  DATABASE EMBL 'Online! Accession Number AF035013, 4 January 1999 (1999-01-04) JIANG Y. AND ZHAO K.: "Homo sapiens cell cycle related kinase mRNA, complete cds." XP002169444 abstract

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

A CONTRACTOR

International application No. PCT/US 00/14842

		<del></del>
Box I	Observations where certain claims were found unsearchable (Continuat	tion of item 1 of first sheet)
This into	nternational Search Report has not been established in respect of certain claims under Arti	ticle 17(2)(a) for the following reasons:
1.	Claims Nos.: because they relate to subject matter not required to be searched by this Authority, name	nely:
2. 🗓	Claims Nos.: 31-34 tsatus F the There to Neuron Are I commanded application to At/2016 to comply with the an extent that no meaningful international Search can be carried out, specifically:	prescribed requirements to such
з. [	Claims Nos.: because they are dependent claims and are not drafted in accordance with the second	
Box II	Observations where unity of invention is lacking (Continuation of item 2	of first sheet)
This int	nternational Searching Authority found multiple inventions in this international application, a see add1t1onal sheet	as follows:
1.	As all required additional search tees were timely paid by the applicant, this International searchable claims.	al Search Report covers all
2.	As all searchable claims could be searched without effort justifying an additional fee, thi of any additional fee.	is Authority did not invite payment
Х 3. 🗀	As only same of the required additional search trees were timely paid by the applicant to obvers only those chambing winds tees with paid paid by the applicant to obvers only those chambing winds tees with paid partially (completely), 23-38 (partially)	his International Search Beport
4.	No required additional search fees were timely paid by the applicant. Consequently, this restricted to the invention first mentioned in the claims; it is covered by claims Nos.:	s International Search Report is
Remari	The additional search fees were ac No protest accompanied the payments	ecompanied by the applicant's protest.

Form PCT/ISA/210 (continuation of first sheet (1)) (July 1998)

BNSDOCID: <WO\_\_\_\_0073469A3\_I\_>

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: Invention 1: Claims 1-14,26-38 (all partially)

A nucleic acid molecule encoding a kinase polypeptide as represented by SEQ.ID.122 or a domain thereof; a vector and a recombinant cell comprising said nucleic acid molecule; a nucleic acid probe for the detection of said nucleic acid molecule; a polypeptide as represented by SEQ.ID.122 or a fragment thereof; an antibody or antibody fragment having specific binding affinity to said polypeptide; a hybridoma which produces said antibody; methods for identifying a substance that modulates the kinase activity of said polypeptide; methods for treating a disease or disorder by administering such a substance; and methods for the detection of a kinase polypeptide as represented by SEQ.ID.122.

Claims: Inventions 2-78: Claims 1-20,
 23-38 (all partially and as far as applicable)

A nucleic acid molecule encoding a kinase with a polypeptide sequence selected from SEQ.IDs. $\overline{1}23-199$ , wherein invention 2 is limited to SEQ.ID. 123, invention 3 is limited to SEQ.ID. 124, ....., and invention 78 is limited to SEQ.ID.199, or a domain thereof; a vector and a recombinant cell comprising said nucleic acid molecule; a nucleic acid probe for the detection of said nucleic acid molecule; a polypeptide as represented by a polypeptide sequence selected from SEQ.IDs.123-199 or a fragment thereof; an antibody or antibody fragment having specific binding affinity to said polypeptide; a hybridoma which produces said antibody; methods for identifying a substance that modulates the kinase activity of said polypeptide; methods for treating a disease or disorder by administering such a substance; and methods for the detection of a kinase polypeptide represented by a polypeptide sequence selected from SEO. IDs. 123-199.

3. Claims: Invention 79: Claim 21 (completely) and Claims 1-14,26-38 (all partially)

A nucleic acid molecule encoding a kinase polypeptide as represented by SEQ.ID.200 or a domain thereof; a vector and a recombinant cell comprising said nucleic acid molecule; a nucleic acid probe for the detection of said nucleic acid molecule; a polypeptide as represented by SEQ.ID.200 or a fragment thereof; an antibody or antibody fragment having

specific binding affinity to said polypeptide; a hybridoma which produces said antibody; methods for identifying a substance that modulates the kinase activity of said polypeptide; methods for treating a disease or disorder by administering such a substance; and methods for the detection of a kinase polypeptide as represented by SEQ.ID.200.

4. Claims: Invention 80: Claim 22 (completely) and Claims 1-14,26-38 (all partially)

A nucleic acid molecule encoding a kinase polypeptide as represented by SEQ.ID.201 or a domain thereof; a vector and a recombinant cell comprising said nucleic acid molecule; a nucleic acid probe for the detection of said nucleic acid molecule; a polypeptide as represented by SEQ.ID.201 or a fragment thereof; an antibody or antibody fragment having specific binding affinity to said polypeptide; a hybridoma which produces said antibody; methods for identifying a substance that modulates the kinase activity of said polypeptide; methods for treating a disease or disorder by administering such a substance; and methods for the detection of a kinase polypeptide as represented by SEQ.ID.201.

5. Claims: Inventions 81-121: Claims 1-20, 23-38 (all partially and as far as applicable)

A nucleic acid molecule encoding a kinase with a polypeptide sequence selected from SEQ.IDs.202-242, wherein invention 81 is limited to SEQ.ID. 202, invention 82 is limited to SEQ.ID. 203, ....., and invention 121 is limited to SEQ.ID.242, or a domain thereof; a vector and a recombinant cell comprising said nucleic acid molecule; a nucleic acid probe for the detection of said nucleic acid molecule: a polypeptide as represented by a polypeptide sequence selected from SEQ.IDs.202-242 or a fragment thereof; an antibody or antibody fragment having specific binding affinity to said polypeptide; a hybridoma which produces said antibody; methods for identifying a substance that modulates the kinase activity of said polypeptide; methods for treating a disease or disorder by administering such a substance; and methods for the detection of a kinase polypeptide represented by a polypeptide sequence selected from SEQ.IDs.202-242.

6. Claims: Inventions 122-136: Claims 15-20, 23-25 (all partially) and claims 1-14, 26-38 (if applicable)

A nucleic acid molecule encoding a kinase polypeptide as represented by a 'gene name' selected from 'AA980090', 'AA045601', 'AA297313', 'N23936', '5R72-18-1', '5R79-54-1', '5R65-16-1', 'AA065538', 'H17727', 'W08549', 'AA430250', 'AA139478', 'R87679', 'W65887', 'AA948538', '5R69-23-3', and '5R69-26-2', wherein invention 122 is limited to 'AA980090', invention 123 is limited to 'AA045601', ..... and invention 136 is limited to '5R69-26-2', or a domain thereof; a vector and a recombinant cell comprising said nucleic acid molecule; a nucleic acid probe for the detection of said nucleic acid molecule; a polypeptide encoded by said nucleic acid molecule or a fragment thereof; an antibody or antibody fragment having specific binding affinity to said polypeptide; a hybridoma which produces said antibody; methods for identifying a substance that modulates the kinase activity of said polypeptide; methods for treating a disease or disorder by administering such a substance; and methods for the detection of a said polypeptide.

page 3 of 3

Continuation of Box I.2

Claims Nos.: 31-34

The search was based on the sequence listing furnished in computer readable form, the numbering of which differs from the numbering in the figures.

Claims 31-34 refer to a 'substance that modulates the activity of a kinase' without giving a true technical characterization. Moreover, no such specific compounds are defined in the application. In consequence, the scope of said claims is ambiguous and vague, and their subject-matter is not sufficiently disclosed and supported (Art. 5 and 6 PCT). No search can be carried out for such purely speculative claims whose wording is, in fact, a mere recitation of the results to be achieved.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

BNSDOCID: <WO\_\_\_\_\_0073469A3\_I\_>

Information on patent family members

Int. .ional Application No
PCT/US 00/14842

Patent documer cited in search rep		Publication date	I	Patent family member(s)	Publication date
WO 0058473	Α	05-10-2000	AU	3774500 A	16-10-2000
WO 0006728	Α	10-02-2000	AU EP	5134999 A 1100904 A	21-02-2000 23-05-2001
WO 9858052	A	23-12-1998	 US	5885803 A	23-03-1999
			AU	8154798 A	04-01-1999
			EP	1007692 A	14-06-2000
			US 	6207148 B	27-03-2001
WO 0055332	Α	21-09-2000	AU	3899600 A	04-10-2000
			AU WO	5034200 A	12-12-2000
				0071679 A	30-11-2000 
WO 9733909	Α	18-09-1997	AU AU	728186 B	04-01-2001
			BR	2329597 A 9708082 A	01-10-1997 27-07-1999
			CA	2249742 A	18-09-1997
			EP .	0914335 A	12-05-1999
			NO	984229 A	13-11-1998
			US 	6034218 A	07-03-2000 
WO 9957144	Α	11-11-1999	AU	3885999 A	23-11-1999
			EP	1075518 A	14-02-2001
WO 9811234	Α	19-03-1998	US	5773699 A	30-06-1998
			US	5863780 A	26-01-1999
			AU Ep	4261197 A 0927257 A	02-04-1998 07-07-1999
			ÜS	6045792 A	04-04-2000
			US	6232077 B	15-05-2001
EP 0861896	Α	02-09-1998	DE	19708173 A	03-09-1998
			CA	2224404 A	28-08-1998
			JP 	10248566 A	22 <b>-</b> 09-1998 
WO 0035946 	A 	22-06-2000	NONE		
WO 9831802	Α	23-07-1998	AU	6031398 A	07-08-1998
			EP	0972026 A	19-01-2000
WO 9950395	Α	07-10-1999	NONE		
WO 9933961	Α	08-07-1999	AU	1691499 A	19-07-1999
WO 9801756	Α	15-01-1998	US	5863729 A	26-01-1999
			AU	3651597 A	02-02-1998
WO 9949062	Α	30-09-1999	AU	3208999 A	18-10-1999
			EP	1073756 A	07-02-2001
WO 9835015	Α	13-08-1998	EP	0972011 A	19-01-2000
			US	5968800 A	19-10-1999
			US 	6030788 A	29-02-2000
WO 9938981	Α	05-08-1999	US	5962232 A	05-10-1999
			AU	2113899 A	16-08-1999
			EP	1051497 A	15-11-2000

information on patent family members

Internal Application No
PCT/US 00/14842

		T			C1/U3	00/14842
Patent document cited in search repor	1	Publication date		atent family member(s)		Publication date
WO 9836054	Α	20-08-1998	AU	5973498	A	08-09-199
WO 9958558	Α	18-11-1999	AU	4077099	Α	29-11-199
			EP	1078057		28-02-200
US 6013455	A	11-01-2000	AU	1315900	Α	01-05-200
			WO	0022143		20-04-200
EP 0870825	A	14-10-1998	US	5965420		12-10-1999
			CA	2231046		05-09-1998
			JР	11000179		06-01-1999
			US	6165766	A	26-12-2000
WO 9405794	Α	17-03-1994	EP	0658204	A	21-06-199
			US	5690930	Α	25-11-1997
WO 0009678	Α	24-02-2000	AU	5491599	A	06-03-2000
WO 0014212	Α	16-03-2000	US	6183962	В	06-02-2001
			AU	5817799	Α	27-03-2000
			บร	6043040	Α	28-03-2000
			US	6146841	Α	14-11-2000
			US	6180358	В	30-01-2001
			US	6153417		28-11-2000
			US	6146832	Α	14-11-2000
			US	6190874	В	20-02-2001
			us	6121030		19-09-2000
			US	6200770		13-03-2001
	~~~~	• • • • • • • • • • • • • • • • • • •	US	6214597	B	10-04-2001
WO 9904265	Α	28-01-1999	US	6218521		17-04-2001
			US	6043084		28-03-2000
			AU	8571598		10-02-1999
			EP	0996857	Α	03-05-2000
WO 0022143	Α	20-04-2000	US	6013455		11-01-2000
			AU	1315900	Α	01-05-2000
WO 9932609	Α	01-07-1999	AU	1991799	• •	12-07-1999
			AU	1991899		12-07-1999
			EP	1037920		27-09-2000
			WO	9932517	A	01-07-1999
EP 1033401	A	06-09-2000	NONE			
WO 9747750	Α	18-12-1997	AU	718792		20-04-2000
			AU	3284297	Α	07-01-1998
			EP	0914451	Α	12-05-1999
				000512147	T	19-09-2000
			NO	985742	A	10-02-1999
WO 9964589	A	16-12-1999	AU	4278299	A	30-12-1999
			ΕP	1084245	Α	21-03-2001

Form PCT/ISA/210 (patent family annex) (July 1992)

THIS PAGE BLANK (USPTO)